

# Dietary Patterns during Lactation and Human Milk Composition and Quantity: A Systematic Review

2020 Dietary Guidelines Advisory Committee, Pregnancy and Lactation Subcommittee

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Nutrition Evidence Systematic Review
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This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee in collaboration with the Nutrition Evidence Systematic Review (NESR) team at the Center for Nutrition Policy and Promotion, Food and Nutrition Service, U.S. Department of Agriculture (USDA). All systematic reviews from the 2020 Advisory Committee Project are available on the NESR website: <a href="https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews">https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews</a>.

Conclusion statements drawn as part of this systematic review describe the state of science related to the specific question examined. Conclusion statements do not draw implications, and should not be interpreted as dietary guidance. This portfolio provides the complete documentation for this systematic review. A summary of this review is included in the 2020 Advisory Committee's Scientific Report available at <a href="https://www.bietaryGuidelines.gov">www.bietaryGuidelines.gov</a>.

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USDA and HHS implemented a process to identify topics and scientific questions to be examined by the 2020 Dietary Guidelines Advisory Committee. The Committee conducted its review of evidence in subcommittees for discussion by the full Committee during its public meetings. The role of the Committee members involved establishing all aspects of the protocol, which presented the plan for how they would examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that met the criteria they set; deliberating on the body of evidence for each question; and writing and grading the conclusion statements to be included in

<sup>&</sup>lt;sup>1</sup> Under contract with the Food and Nutrition Service, United States Department of Agriculture.

the scientific report the 2020 Committee submitted to USDA and HHS. The NESR team with assistance from Federal Liaisons and Project Leadership, supported the Committee by facilitating, executing, and documenting the work necessary to ensure the reviews were completed in accordance with NESR methodology. More information about the 2020 Dietary Guidelines Advisory Committee, including the process used to identify topics and questions, can be found at <a href="https://www.DietaryGuidelines.gov">www.DietaryGuidelines.gov</a>. More information about NESR can be found at <a href="https://www.DietaryGuidelines.gov">NESR.usda.gov</a>.

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### INTRODUCTION

This document describes a systematic review conducted to answer the following question: What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity? This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee, supported by USDA's Nutrition Evidence Systematic Review (NESR).

More information about the 2020 Dietary Guidelines Advisory Committee is available at the following website: <a href="https://www.DietaryGuidelines.gov">www.DietaryGuidelines.gov</a>.

NESR specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. More information about NESR is available at the following website: NESR.usda.gov.

NESR's systematic review methodology involves developing a protocol, searching for and selecting studies, extracting data from and assessing the risk of bias of each included study, synthesizing the evidence, developing conclusion statements, grading the evidence underlying the conclusion statements, and recommending future research. A detailed description of the systematic reviews conducted for the 2020 Dietary Guidelines Advisory Committee, including information about methodology, is available on the NESR website: <a href="https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews">https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews</a>. In addition, starting on page 62, this document describes the final protocol as it was applied in the systematic review. A description of and rationale for modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 3. Food, Beverage, and Nutrient Consumption During Lactation.

## List of abbreviations

Abbreviation	Full name
AMDR	Acceptable Macronutrient Distribution Range
СНО	Carbohydrate
DHA	Docosahexaenoic acid
EPA	Eicosapentaenoic acid
HDI	Human Development Index
HHS	Department of Health and Human Services
MUFA	Monounsaturated fatty acid
NESR	Nutrition Evidence Systematic Review
PUFA	Polyunsaturated fatty acid
PRO	Protein
RCT	Randomized controlled trial
SAT	Saturated fat
SES	Socioeconomic status
slgA	Secretory immunoglobulin A
USDA	United States Department of Agriculture

# WHAT IS THE RELATIONSHIP BETWEEN DIETARY PATTERNS CONSUMED DURING LACTATION AND HUMAN MILK COMPOSITION AND QUANTITY?

#### PLAIN LANGUAGE SUMMARY

## What is the question?

• The question is: What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity?

## What is the answer to the question?

- No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk quantity.
- Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distributions during lactation and human milk quantity.
- Insufficient evidence is available to determine the relationship between dietary patterns during lactation and total fat in human milk.
- Limited evidence suggests that maternal consumption of diets higher in fat (>35 percent fat) and lower in carbohydrate during lactation is related to higher total fat in human milk collected in the maternal postprandial period.
- Limited evidence suggests that certain maternal dietary patterns during lactation, including diets based on macronutrient distributions, are related to the relative proportions of saturated fat and monounsaturated fatty acids in human milk, and of polyunsaturated fatty acids in human milk collected in the maternal postprandial period.
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and total protein concentration in human milk.
- Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distribution during lactation and total protein concentration in human milk.
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and bioactive proteins including alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, secretory immunoglobulin A, lysozyme in human milk.
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk oligosaccharides.
- Insufficient evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamin B<sub>12</sub> concentration in human milk.
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamin C, choline and B vitamins (other than vitamin B<sub>12</sub>) in human milk.
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamins A, D, E and K in human milk.
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and iodine and selenium in human milk.

## Why was this question asked?

 This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.

## How was this question answered?

- The 2020 Dietary Guidelines Advisory Committee, Pregnancy and Lactation Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- Dietary patterns were defined as the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.
- Diets based on macronutrient distribution were examined when at least one
  macronutrient proportion was outside of the acceptable macronutrient distribution
  range (AMDR) for carbohydrate, fat, and/or protein, whether or not the foods/food
  groups consumed were provided.

## What is the population of interest?

- For the question on dietary patterns and human milk composition, the population of interest is generally healthy, lactating women.
- For the question on dietary patterns and human milk quantity, the population of interest is generally healthy, lactating women who are exclusively or predominantly feeding their child human milk.

#### What evidence was found?

- This review includes seven articles published between 2009 and 2019.
- Two studies reported that a maternal diet higher in fat during lactation (i.e., more than 35 percent of total energy from fat, which is greater than the acceptable macronutrient distribution range resulted in higher total fat in human milk).
- Some studies showed that maternal dietary patterns during lactation were related to the relative proportions of saturated fat, monounsaturated fatty acids, and polyunsaturated fatty acids in human milk, which differed depending on whether milk samples were collected in a fed or fasted state.
- The body of evidence is limited in several ways:
  - Small sample sizes of the studies.
  - Inconsistencies in when and how human milk was collected across studies.
  - Concerns about potential bias of the studies, including the possibility that factors other than maternal diet impacted the outcomes.
  - Study populations that are not representative of the racial/ethnic or socioeconomic diversity of the U.S.
- There was insufficient or no evidence to assess the relationship between maternal dietary patterns during lactation and several outcomes, including human milk quantity and composition of total protein, water soluble vitamins (B, C, and choline), fat soluble vitamins (A, D, E, and K), minerals (iodine and selenium), human milk oligosaccharides, and bioactive proteins (alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, secretory immunoglobulin A, and lysozyme).

# How up-to-date is this systematic review?

• This review searched for studies from January 2000 to November 2019.

### TECHNICAL ABSTRACT

## Background

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.
- The 2020 Dietary Guidelines Advisory Committee, Pregnancy and Lactation Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- The goal of this systematic review was to examine the following question: What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity?

## **Conclusion statements and grades**

- No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk quantity. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between maternal n differing in macronutrient distributions during lactation and human milk quantity. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between dietary patterns during lactation and total fat in human milk. (Grade: Grade not assignable)
- Limited evidence suggests that maternal consumption of diets higher in fat (>35 percent fat) and lower in carbohydrate during lactation is related to higher total fat in human milk collected in the maternal postprandial period. (Grade: Limited)
- Limited evidence suggests that certain maternal dietary patterns during lactation, including diets based on macronutrient distributions, are related to the relative proportions of saturated fat and monounsaturated fatty acids in human milk, and of polyunsaturated fatty acids in human milk collected in the maternal postprandial period. (Grade: Limited)
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and total protein concentration in human milk. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distribution during lactation and total protein concentration in human milk. (Grade: Grade not assignable)
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and bioactive proteins including alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, secretory immunoglobulin A, lysozyme in human milk. (Grade: Grade not assignable)
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk oligosaccharides. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamin B<sub>12</sub> concentration in human milk. (Grade: Grade not assignable)
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamin C, choline and B vitamins (other than vitamin

- B<sub>12</sub>) in human milk. (Grade: Grade not assignable)
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamins A, D, E and K in human milk. (Grade: Grade not assignable)
- No evidence is available to determine the relationship between maternal dietary patterns during lactation and iodine and selenium in human milk. (Grade: Grade not assignable)

#### Methods

- A literature search was conducted using four databases (PubMed, Cochrane, Embase, and CINAHL) to identify articles that evaluated the intervention or exposure of dietary patterns during lactation and the outcomes of human milk composition and quantity. A manual search was conducted to identify articles that may not have been included in the electronic databases searched. Articles were screened by two NESR analysts independently for inclusion based on predetermined criteria.
- Data extraction and risk of bias assessment were conducted for each included study, and both were checked for accuracy. The Committee qualitatively synthesized the body of evidence to inform development of conclusion statements, and graded the strength of evidence using pre-established criteria for risk of bias, consistency, directness, precision, and generalizability.

## Summary of the evidence

- This systematic review includes three randomized controlled trials (RCTs) (four articles) and two cross-sectional studies (three articles) published between 2009 and 2019.
- Studies included in this review assessed one of the following maternal interventions or exposures during lactation:
  - Dietary patterns (2 studies)
  - Diets based on macronutrient distributions outside of the acceptable macronutrient distribution range (AMDR) (3 studies)
- Two of the three RCTs reported that a maternal diet higher in fat during lactation (i.e., >35 percent of total energy from fat, which is greater than the AMDR) resulted in higher total fat in human milk.
- Some, but not all studies showed that maternal dietary patterns during lactation were related to the relative proportions of saturated fat (SAT), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) in human milk, which differed depending on whether milk samples were collected in a fed or fasted state.
- This body of evidence had notable limitations:
  - All RCTs had a small sample size (<20 participants) and none reported power analyses.
  - o The cross-sectional studies did not account for most of the confounders.
  - One cross-sectional study reported that the participants differed on supplement intake during lactation, in addition to differing on dietary patterns. However, this was not controlled for in the statistical analysis or accounted for in the interpretation of the study findings.
  - o The timing and methods of human milk collection were heterogeneous.

- The study populations did not represent the racial/ethnic or socioeconomic diversity of the U.S. population.
- Insufficient or no evidence was available to assess the association between dietary patterns and several other outcomes, including human milk quantity and human milk composition of total protein, water soluble vitamins (B, C, and choline), fat soluble vitamins (A, D, E, and K), minerals (iodine and selenium), human milk oligosaccharides, and bioactive proteins (alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, secretory immunoglobulin A (slgA), and lysozyme).

#### **FULL REVIEW**

## Systematic review question

What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity?

## **Conclusion statements and grades**

No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk quantity. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distributions during lactation and human milk quantity. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between dietary patterns during lactation and total fat in human milk. (Grade: Grade not assignable)

Limited evidence suggests that maternal consumption of diets higher in fat (>35 percent fat) and lower in carbohydrate during lactation is related to higher total fat in human milk collected in the maternal postprandial period. (Grade: Limited)

Limited evidence suggests that certain maternal dietary patterns during lactation, including diets based on macronutrient distributions, are related to the relative proportions of saturated fat and monounsaturated fatty acids in human milk, and of polyunsaturated fatty acids in human milk collected in the maternal postprandial period. (Grade: Limited)

No evidence is available to determine the relationship between maternal dietary patterns during lactation and total protein concentration in human milk. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between maternal diets differing in macronutrient distribution during lactation and total protein concentration in human milk. (Grade: Grade not assignable)

No evidence is available to determine the relationship between maternal dietary patterns during lactation and bioactive proteins including alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, secretory immunoglobulin A, lysozyme in human milk. (Grade: Grade not assignable)

No evidence is available to determine the relationship between maternal dietary patterns during lactation and human milk oligosaccharides. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamin B<sub>12</sub> concentration in human milk. (Grade: Grade not assignable)

No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamin C, choline, and B vitamins (other than vitamin B<sub>12</sub>) in human milk. (Grade: Grade not assignable)

No evidence is available to determine the relationship between maternal dietary patterns during lactation and vitamins A, D, E, and K in human milk. (Grade: Grade not

assignable)

No evidence is available to determine the relationship between maternal dietary patterns during lactation and iodine and selenium in human milk. (Grade: Grade not assignable)

## Summary of the evidence

- This systematic review includes three randomized controlled trials (RCTs) (four articles)<sup>1-4</sup> and two cross sectional studies (three articles)<sup>5-7</sup> published between 2009 and 2019.
- Studies included in this review assessed one of the following maternal interventions or exposures during lactation:
  - Dietary patterns (2 studies)
  - Diets based on macronutrient distributions outside of the acceptable macronutrient distribution range (AMDR) (3 studies)
- Two of the three RCTs reported that a maternal diet higher in fat during lactation (i.e., >35 percent of total energy from fat, which is greater than the AMDR) resulted in higher total fat in human milk.
- Some, but not all studies showed that maternal dietary patterns during lactation were related to the relative proportions of saturated fat (SAT), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) in human milk, which differed depending on whether milk samples were collected in a fed or fasted state.
- This body of evidence had notable limitations:
  - All RCTs had a small sample size (<20 participants) and none reported power analyses.
  - The cross-sectional studies did not account for most of the confounders.
  - One cross-sectional study reported that the participants differed on supplement intake during lactation, in addition to differing on dietary patterns. However, this was not controlled for in the statistical analysis or accounted for in the interpretation of the study findings.
  - o The timing and methods of human milk collection were heterogeneous.
  - The study populations did not represent the racial/ethnic or socioeconomic diversity of the U.S. population.
- Insufficient or no evidence was available to assess the association between
  dietary patterns and several other outcomes, including human milk quantity and
  human milk composition of total protein, water soluble vitamins (B, C, and
  choline), fat soluble vitamins (A, D, E, and K), minerals (iodine and selenium),
  human milk oligosaccharides, and bioactive proteins (alpha-lactalbumin,
  lactoferrin, casein, alpha (1) antitrypsin, osteopontin, secretory immunoglobulin
  A (slgA), and lysozyme).

## **Description of the evidence**

This systematic review included articles that address the relationship between dietary patterns and/or diets based on macronutrient distributions during lactation and human milk composition and quantity. The search included articles from countries categorized as high or very high on the Human Development Index (HDI)<sup>ii</sup> and published from January 2000 to November 2019. Studies included generally healthy women during lactation at the time of the intervention or exposure. The following study designs were included: RCTs, non-randomized controlled trials, prospective and retrospective cohort studies, nested case-control studies, and cross-sectional studies. Due to changes in human milk composition during the first weeks after delivery, only studies assessing milk composition in mature milk (defined as milk produced ≥14 days postpartum) were included.

Dietary pattern was defined as the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they were habitually consumed. At a minimum, there had to be a description of the foods and beverages in the pattern. It may have been measured or derived using a variety of approaches, such as adherence to a priori patterns (indices/scores), data driven patterns (factor or cluster analysis), reduced rank regression, or other methods, including clinical trials.

Studies assessing diets based on macronutrient distributions outside of the AMDR had to include the macronutrient distribution of carbohydrate, fat, and protein of the diet, and include at least one macronutrient outside of the AMDR. Macronutrient percentages of energy outside of the AMDR are as follows:

- Carbohydrate for all age groups: < 45 or > 65 percent of energy;
- Protein for ≥ 19 years: < 10 or > 35 percent of energy;
- Fat for ≥ 19 years: < 20 or > 35 percent of energy

The outcomes considered in this review were human milk composition (specifically, macronutrients (fatty acids and total protein), water soluble vitamins (B, C, and choline), fat soluble vitamins (A, D, E, and K), selected minerals (iodine and selenium), human milk oligosaccharides, selected bioactive proteins (alpha-lactalbumin, lactoferrin, casein, alpha (1) antitrypsin, osteopontin, slgA, lysozyme) and human milk quantity.

In total, seven articles from five different studies were included in the body of evidence. The evidence in this review is presented based on the exposure: 1) Dietary patterns;

-

The Human Development classification was based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data were collected (UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: <a href="http://hdr.undp.org/en/data">http://hdr.undp.org/en/data</a>). If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank was used instead (The World Bank. World Bank country and lending groups. Available from:

2) Diets based on macronutrient distributions.

## **Dietary patterns**

The baseline characteristics and study findings are presented in **Table 1** and **Table 2**. Three articles from two cross-sectional studies assessed the association between dietary patterns during pregnancy and human milk composition.<sup>5-7</sup> One study was conducted in the U.S. and produced two articles from the same sample<sup>5,6</sup> and another study was conducted in China.<sup>7</sup> The baseline sample sizes in the China<sup>7</sup> and the U.S. studies<sup>5,6</sup> were 287 and 74, respectively.

The participants in the U.S. study were predominantly White, well-educated and had a mean age of 32 years. The Chinese study participants had a mean age of 29.8 years, were 100 percent Chinese Han, and were predominantly from middle-to-higher income households. Mean prepregnancy BMI in the Chinese study was 20.6 kg/m². In the U.S. study, the mean prepregnancy BMI was higher, though mostly within the healthy range, and there was a significant difference between the comparison groups, with vegans (22.8 kg/m²) having the lowest BMI when compared to vegetarians (23.9 kg/m²) and omnivores (25.8 kg/m²).

The Chinese study<sup>7</sup> used a factor/cluster analysis to arrive at the following dietary patterns:

- Pattern 1: Mushroom food and algae, Meat, Marine products
- Pattern 2: Soybean products, Nuts, Dairy
- Pattern 3: Fruit, Vegetables
- Pattern 4: Grain/potato and beans, Eggs

In the U.S. study,<sup>5,6</sup> during initial screening, participants self-identified their dietary pattern as vegan, vegetarian, or omnivore dietary patterns. Subsequently, a diet survey was administered to the enrolled participants, based on which the following dietary patterns were identified:

- Vegan: Never consumed meat and never or rarely consumed other animal products
- Vegetarian: Never or rarely consumed meat and sometimes or often consumed other animal products
- Omnivores: Consumed meat sometimes or often

All three articles assessed human milk composition. Specifically, two articles<sup>6,7</sup> assessed fatty acid composition in human milk and one<sup>5</sup> assessed vitamin B<sub>12</sub> levels in human milk. None of the articles assessed human milk quantity.

#### Diets based on macronutrient distributions

Three RCTs<sup>1-4</sup> assessed the association between diets based on macronutrient distributions and human milk composition and quantity. Two studies were conducted in the U.S.<sup>1,2,4</sup> and one in Canada.<sup>3</sup> The sample sizes in these studies were small, with < 20 participants in each study.

The mean age of the participants in the RCTs ranged from 27 years<sup>4</sup> to 31.6 years.<sup>3</sup> Maternal BMI was mostly within the healthy range, except for the study by Nasser et al,<sup>3</sup> in which a mean BMI of 26 kg/m<sup>2</sup> was reported. Only Mohammad et al<sup>1,2</sup> reported race/ethnicity, noting that the study included 2 White, 2 African American, and 3

Hispanic mothers.

All RCTs that assessed diets based on macronutrient distributions were crossover studies that manipulated macronutrient percentage of energy above or below the AMDR for both fat and carbohydrate<sup>1-3</sup> or fat<sup>4</sup> only.

- Mohammad et al<sup>1,2</sup> (baseline n=7) randomized mothers to a "H-F" diet (30 percent carbohydrate, 55 percent fat, 15 percent protein) or a "H-CHO" diet (60 percent carbohydrate, 25 percent fat, 15 percent protein) for 8 days each with a washout period of 1-2 weeks. In the "H-F" diet group, the percentage of energy from carbohydrate was below the AMDR and energy from fat was above the AMDR, whereas, in the "H-CHO" diet, both carbohydrate and fat were within the percentage of energy ranges of the AMDR.
- Nasser et al<sup>3</sup> (baseline n=14) randomized mothers to a "high fat" diet (HF: 40.3 percent fat, 45.3 percent carbohydrate, 14.4 percent protein) or "low fat" diet (LF: 17.6 percent fat, 68 percent carbohydrate, 14.4 percent protein) diet for 4 days each, with a washout period of 3 days. In the "high fat" diet, percent of energy from fat was above the AMDR while percentage of energy from carbohydrates was within the AMDR; in the "low fat" diet, percentage of energy from fat was outside the AMDR and percentage of energy from carbohydrate was above the AMDR.
- Yahvah et al<sup>4</sup> (baseline n=16) randomized mothers to a "low-fat dairy" (24 percent fat) or "full-fat dairy" (36 percent fat) diet for 14 days each with a 14 day washout period. The percentage of energy from fat was above the AMDR in the "full-fat dairy group;" the percentage of energy from fat in the "low-fat dairy" group was within the AMDR and percentage of energy from both carbohydrate and protein were within the AMDR for both dairy groups.

All of the RCTs assessed human milk composition<sup>2-4</sup> and only one study assessed both human milk composition and quantity.<sup>1</sup> The studies primarily measured total fat and fatty acid in human milk,<sup>2-4</sup> although one study also measured protein content.<sup>1</sup>

## **Evidence synthesis**

With three RCTs<sup>1-4</sup> and two cross-sectional studies,<sup>5-7</sup> there is a smaller body of evidence available to examine the relationship between dietary patterns during lactation and human milk composition. Only one study<sup>1</sup> assessed the relationship between diets based on macronutrient distributions during lactation and human milk quantity. Below, the results are grouped by two types of exposures – dietary patterns and diets based on macronutrient distributions.

## **Dietary patterns**

Both studies that assessed dietary patterns were cross-sectional studies. Tian et al<sup>7</sup> and Perrin et al<sup>6</sup> assessed the association between dietary patterns and human milk fatty acids (**Table 3**). Pawlak et al<sup>5</sup> was the only study that assessed vitamin B<sub>12</sub> status in human milk. The findings are discussed below.

## Dietary patterns and human milk fatty acids

Tian et al<sup>7</sup> noted significant differences in proportions of certain fatty acids in human milk between women adhering to different dietary patterns. For example, women

adhering to pattern 2 (soybean products, nuts, dairy) and pattern 4 (grain/potato and beans, eggs) had the same average amount of saturated fatty acids in human milk, which was significantly higher than the average among women who adhered to pattern 3 (fruit, vegetables) (p<0.001). Among the four groups, the proportion of PUFAs in milk was the highest in women adhering to pattern 3 and lowest in those adhering to pattern 2 (p=0.025). Similarly, the proportion of omega-6 fatty acids in milk was highest in mothers adhering to pattern 1 (mushroom food and algae, meat, marine products) and lowest in those adhering to pattern 2 (p=0.038). There were no statistically significant differences in omega-3 fatty acids, omega-6 to omega-3 ratios, or proportion of MUFAs in the milk of mothers adhering to different dietary patterns, although the last of these indices approached significance (p=0.053).

Perrin et al<sup>6</sup> reported significant differences in human milk composition between mothers adhering to different dietary patterns. Specifically, milk from mothers adhering to a vegan dietary pattern, when compared to that of mothers adhering to vegetarian or non-vegetarian dietary patterns, had significantly higher unsaturated fatty acids (p<0.001) and total omega-3 fatty acids (p<0.001), and lower saturated fat (p<0.001), trans fat (p<0.001), omega-6 to omega-3 ratios (p<0.001) and linoleic acid to  $\alpha$ -linolenic acid ratios (p<0.001). The significant difference in omega-3 fatty acids was driven by a higher percentage of  $\alpha$ -linolenic acid, with no difference noted in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) across different maternal dietary patterns. Similarly, there were no differences in omega-6 fatty acids (except  $\gamma$ -linolenic acid), total long chain, or total medium chain fatty acids by maternal dietary patterns.

**Summary**: The studies discussed above were heterogeneous in dietary patterns methodology. Specifically, Tian et al<sup>7</sup> used factor analysis to arrive at the dietary patterns, whereas Perrin et al<sup>6</sup> used an 'other' method that relied on grouping women into their respective patterns based on their response to a diet survey. Both studies reported that saturated fat and some of the unsaturated fat in human milk varied significantly across dietary patterns, but the heterogeneity between studies in terms of both the dietary patterns and fatty acid assessment preclude a true comparison and pooling of the study findings.

#### Dietary patterns and human milk vitamin B<sub>12</sub>

Pawlak et al<sup>5</sup> assessed human milk vitamin B<sub>12</sub> levels in women adhering to who vegan, vegetarian and non-vegetarian dietary patterns. There were no significant differences in the vitamin B<sub>12</sub> levels in human milk across these three groups. Thirteen of the 74 women had low vitamin B<sub>12</sub> concentration (< 310 pmol/L) in human milk, although this did not differ by dietary pattern. Similarly, eight women had human milk vitamin B<sub>12</sub> above the assay detection threshold (> 1122 pmol/L), and there was no significant difference between the groups. An important context to consider is that almost half of the vegan women (46.2 percent) consumed vitamin B<sub>12</sub> supplements, whereas only 27.3 percent and 3.9 percent of the vegetarian and non-vegetarian women, respectively, consumed supplements (p=0.001). However, this was not accounted for in the analysis.

### Diets based on macronutrient distributions

All studies that assessed diets based on macronutrient distributions were RCTs. In terms of outcomes, only one study assessed human milk quantity. All three studies

looked at the association between macronutrient distribution in the diet and human milk fatty acids and the findings are discussed below by individual study, and followed by the synthesis (**Table 4**).

Mohammad et al,<sup>1</sup> the only study that assessed human milk quantity, concluded that there was no significant difference in human milk production in mothers when consuming a "H-CHO" diet (60 percent carbohydrate, 25 percent fat, 15 percent protein) vs. "H-F" diet (30 percent carbohydrates, 55 percent fat and 15 percent protein). There was also no significant effect of the diet on protein in human milk. However, the milk fat concentration and milk fat content per day was significantly higher when consuming "H-F" diet (p<0.05).

Mohammad et al² reported that the total fat in human milk was significantly higher with the "H-F" diet (30 percent carbohydrates, 55 percent fat and 15 percent protein), when compared to the "H-CHO" diet (60 percent carbohydrate, 25 percent fat, 15 percent protein), but this was only observed in the fed state and not after overnight fasting Human milk  $\Sigma$ C2:C14 fatty acid content differed significantly and was mostly higher when women consumed the "H-CHO" vs. "H-F" diet, during both fasted and fed states. Specifically, saturated fatty acids during fed (C4:0, C6:0, C8:0, C10:0, C12:0, C14:0, C16:0 and C18:0) and fasted states (C4:0, C6:0, C8:0, C10:0, C14:0) were higher in the milk of the mothers during the "H-CHO" diet, as opposed to the "H-F" diet. Despite the differences in individual saturated fatty acids,  $\Sigma$ SAT was not significantly higher when women consumed either the "H-CHO" or "H-F" diet, irrespective of being in fed or fasted states. However, the percent total fat of  $\Sigma$ SAT in human milk was significantly higher during the "H-CHO" diet in the fed state only.

Human milk ∑MUFA was significantly higher when women consumed the "H-F" diet as opposed to the "H-CHO" diet, in the fed state. There was, however, no difference in the fasted state. The percent total fat of ∑MUFA was significantly higher during the "H-F" diet in both fed and fasted states. Similarly, women during their "H-F" diet had higher milk ∑PUFA (specifically C20:2, C20:3, C20:4, C20:5, C22:6) when compared to the "H-CHO" diet. This difference was noted only in the fed state and not in the fasted state. No statistically significant differences were observed in the percent total fat of ∑PUFA when consuming "H-CHO" vs. "H-F" diets, in both fed and fasted states.

Nasser et al³ noted no significant differences in the mean total concentrations of saturated fatty acids, MUFA, and PUFA when women were consuming the "low fat" (68 percent carbohydrate, 17.6 percent fat, 14.4 percent protein) vs. "high fat" diet (45.3 percent carbohydrate, 40.3 percent fat 14.4 percent protein). However, the concentrations of total medium chain fatty acids (C8:0-C14:0) were significantly higher during the "low fat" vs. "high fat" diet (p=0.01). Similarly, certain n-6 fatty acids ( $\gamma$ -linolenic acid, dihomo-  $\gamma$ -linolenic acid, and arachidonic acid) were significantly higher with the "low fat" diet when compared to the "high fat" diet.  $\alpha$ -linolenic acid (C18:3n-3) in milk was higher when mothers consumed the "high fat" vs. "low fat" diet.

Yahvah et al<sup>4</sup> reported that the total lipids in human milk were significantly higher with a "full-fat dairy" diet (48 percent carbohydrate, 36 percent fat, 17 percent protein) when compared to a "low-fat dairy" diet (57 percent carbohydrates, 24 percent fat, 20 percent protein). Saturated fat was higher in the milk of women consuming a "full-fat dairy" diet vs. "low-fat dairy" diet (specifically, C12:0, C13:0, iso-C14:0, C15:0, iso-C15:0, anteiso-C15:0, C16:0, iso-C16:0, C17:0, iso-C17:0, anteiso-C17:0, C18:0,

anteiso 18:0, iso-18:0, C20:0). Many of the MUFAs in the milk did not differ based on the intervention, with the exception of C14:1, C16:1t9, and C18:1t11, which were higher in the milk of women consuming the full-fat dairy diet. Most of the PUFAs varied with the dietary intervention, with C16:2 and C18:2 c9,t11 higher in milk after women had the "full-fat dairy" diet; on the other hand,  $\alpha$ -linolenic acid was higher in milk after women had the "low-fat dairy" diet.

**Summary**: Across four articles, Mohammad et al<sup>1</sup> was the only study that reported human milk quantity and there was no statistically significant relationship between diet macronutrient distribution and human milk volume. Mohammad et al (2009)<sup>1</sup> and Mohammad et al (2014)<sup>2</sup> (both from the same trial) and Yahvah et al<sup>4</sup> reported that total milk fat was higher after consuming the "H-F" diet or the "full-fat dairy" diet.

- Saturated fatty acid: Both Mohammad et al<sup>2</sup> and Nasser et al<sup>3</sup> reported no differences in total saturated fatty acids. However, when mothers consumed a "H-CHO" diet (60 percent carbohydrate, 25 percent fat, 15 percent protein)<sup>2</sup> or a "low fat" diet (68 percent carbohydrate, 17.6 percent fat, 14.4 percent protein)<sup>3</sup>, their milk was higher in certain individual saturated fatty acids (Table 4). Yahvah et al<sup>4</sup> did not report total saturated fatty acids, but noted that certain saturated fatty acids were higher when mothers consumed the "low-fat dairy" diet (57 percent carbohydrate, 24 percent fat, 20 percent protein) and others were higher when they consumed the "full-fat dairy" diet (48 percent carbohydrate, 36 percent fat, 17 percent protein).
- MUFAs: Mohammad et al² reported that after the "H-F" diet (30 percent carbohydrates, 55 percent fat and 15 percent protein), human milk was significantly higher in MUFAs. Nasser et al³ reported no differences in total MUFAs in milk when mothers consumed the "low fat" (68 percent carbohydrate, 17.6 percent fat, 14.4 percent protein) vs. "high fat" diet (45.3 percent carbohydrate, 40.3 percent fat 14.4 percent protein), but noted that palmitoleic acid (C16:0) was higher during the "low fat" diet and arachidic acid (C20:0) was higher during the "high fat" diet. Yahvah et al⁴ did not report total MUFAs, but noted that when mothers consumed the "full-fat dairy" diet (48 percent carbohydrate, 36 percent fat, 17 percent protein), their milk was higher in certain MUFAs (C14:1, C16:1t, C18:1t11), whereas C12:0 and iso-17:0 was higher with the "low-fat dairy" diet (57 percent carbohydrates, 24 percent fat, 20 percent protein).
- **PUFAs:** Mohammad et al² reported that after mothers consumed the "H-F" diet (30 percent carbohydrate, 55 percent fat and 15 percent protein), human milk was significantly higher in PUFAs. Nasser et al³ reported no differences in total PUFAs in human milk when mothers consumed the "low fat" (68 percent carbohydrate, 17.6 percent fat, 14.4 percent protein) vs. "high fat" diet (45.3 percent carbohydrate, 40.3 percent fat, 14.4 percent protein), but noted that mothers had higher α-linolenic acid (C18:3n-3) in milk when consuming the latter diet. On the other hand, γ-linoleic acid (C18:3n-6), dihomo γ-linoleic acid (C20:3n-6), and arachidonic acid (C20:4n-6) were higher when mothers consumed the "low fat" diet. Yahvah et al⁴ did not report total PUFAs, but noted that the milk of mothers consuming the "low-fat dairy" diet (57 percent carbohydrate, 24 percent fat, 20 percent protein) had higher linoleic acid (C18:2) and α-linolenic acid (C18:3n:3).

### Assessment of the evidenceiii

The following conclusion statement was supported by three RCTs and was graded "limited." The individual grading elements are discussed below and summarized in **Table 5.** 

"Limited evidence suggests that maternal consumption of diets higher in fat (>35 percent fat) and lower in carbohydrate during lactation is related to higher total fat in human milk collected in the maternal postprandial period."

As outlined and described below, the body of evidence examining diets based on macronutrient distributions during lactation and human milk composition was assessed for the following elements used when grading the strength of evidence.

• Risk of bias was graded as limited

Agricultural Research Service, Washington, DC.

- Study Design: All studies included in this body of evidence were RCTs, but minimal information on participant randomization methods was reported. Other factors such as maternal BMI and nutritional status prior to enrollment could have influenced the study findings, but are not discussed or accounted for in the articles.
- Intervention/Exposure: Although all 3 RCTs were designed to assess the impact of maternal diet (manipulating outside of AMDR) on human milk fat composition, articles reported minimal information on the foods and types of fat in the intervention diets. Little information was provided on supplement use and the potential influence on the study findings.
- Outcome: There was variability across studies in how and when milk was collected. For example, Mohammad et al<sup>1,2</sup> collected milk when mothers were in fed and fasted states and Mohammad et al<sup>2</sup> presented the results stratified by those two states. However, none of the other studies clarified the maternal fed state during milk collection, thus making it difficult to compare the study findings. Studies also differed on how milk was collected. For example, Nasser et al<sup>3</sup> reported that hind milk was collected, Yahvah et al<sup>4</sup> reported complete extraction of milk from one breast, and Mohammad et al<sup>1,2</sup> noted that 2.5 milliliters was extracted at the beginning, middle, and end of each feeding.
- Timing: The stage of lactation was somewhat different between the studies. While lactation stage of women in the Mohammad et al<sup>1,2</sup> and Nasser et al<sup>3</sup> studies overlapped (6 to 14 weeks and 2 to 6 months postpartum, respectively), Yahvah et al<sup>4</sup> recruited women who were at least 4 months postpartum and the upper bound was not specified.
- Consistency was graded as moderate. Two of the three RCTs noted a
  significant relationship between a higher fat diet and higher total fat in human
  milk. The remaining study<sup>3</sup> noted that the average fat content (assessed in the
  hind milk) was non-significantly greater in the higher fat diet, which is consistent

iii A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: <a href="https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews">https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews</a> and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture,

- with other findings.
- Directness was graded as strong. These RCTs were designed to address the
  question on the relationship between diets with macronutrient distributions
  outside of the AMDR and human milk composition and quantity. Thus, the
  primary objectives of the studies aligned well with the systematic review
  question.
- Precision was graded as limited. All the three RCTs each had a small sample size (<20 participants) and none reported power analyses. Despite this, the magnitude and direction of the results were consistent across studies (as discussed above). None of the studies unduly influenced the findings of this systematic review and removing a single study from the body of evidence would unlikely change the conclusions.
- Generalizability was graded as limited. The studies included in this body of
  evidence were conducted in the U.S. and Canada. However, none of them
  reported the socioeconomic status (SES) of the participants and Nasser et al<sup>3</sup>
  and Yahvah et al<sup>4</sup> did not report the race/ethnicity of participants. Considering
  the small sample size of the RCTs and lack of information on SES and
  race/ethnicity, it is unclear whether the studies were representative of the
  general U.S. population.

The following conclusion statement is supported by three RCTs and two crosssectional studies. The individual grading elements are discussed below and summarized in **Table 5** and **Table 6**.

"Limited evidence suggests that certain maternal dietary patterns during lactation, including diets based on macronutrient distributions, are related to the relative proportions of saturated fat and monounsaturated fatty acids in human milk, and of polyunsaturated fatty acids in human milk collected in the maternal postprandial period."

As outlined and described below, the body of evidence examining dietary patterns during lactation, including diets based on macronutrient distributions, and human milk composition was assessed for the following elements used when grading the strength of evidence.

- Risk of bias was graded limited for the RCTs and limited for the cross-sectional studies. The following bullets address the risk of bias for the 2 cross-sectional studies. For the RCTs, the readers are referred to the risk of bias in the previous section, as the same RCTs contributed to the evidence for both conclusion statements.
  - Study Design: Both Tian et al<sup>7</sup> and Perrin et al<sup>6</sup> selected participants using convenience sampling, which may have introduced selection bias. Related to participant selection, Perrin et al<sup>6</sup> noted that nearly half of the participants (approximately 43 percent) who were invited to participate did not respond and it is unclear whether their baseline characteristics were different from those of women who participated. The mothers in the Perrin et al<sup>6</sup> study also differed significantly by diet group in baseline BMI, which could have influenced the study findings. Tian et al<sup>7</sup> did not adjust for a majority of key confounders and Perrin et al<sup>6</sup> accounted for none of the key confounders identified in the analytic framework.

- by Perrin et al,<sup>6</sup> participants self-reported their dietary data based on a questionnaire that collected information on certain foods and food groups. Also, it is unclear if the questionnaires used in either study were validated. In the Perrin et al study<sup>6</sup>, there were statistically significant differences in maternal DHA/EPA supplement intake between groups (vegan: 26.9 percent, vegetarian: 9.1 percent, omnivore: 3.9 percent), in addition to consuming different dietary patterns. However, this was not accounted for in the analysis and made it difficult to determine the effect of the dietary pattern.
- Outcome: Milk was collected at a single time point. Although milk was collected mid-morning in both the studies, it is unclear whether mothers were in fed or fasted states at the time of collection. Similar to RCTs, both studies differed on how milk was collected. For example, Perrin et al<sup>6</sup> noted that participants provided samples by complete expression of a single breast, whereas, Tian et al<sup>7</sup> reported that 30 milliliters of milk was collected from study participants.
- Timing: The stage of lactation within and between studies varied widely. For example, mothers in the Tian et al<sup>7</sup> study were 22 days to 6 months postpartum at the time of data collection. Perrin et al<sup>6</sup> reported a statistically significant difference in the stage of lactation between exposure groups, ranging from 27.5 to 54.6 weeks postpartum.
- Consistency was graded as moderate for the RCTs and the cross-sectional studies were given a 'grade not assignable' rating. While the studies consistently noted associations between maternal dietary patterns/diets based on macronutrient distributions and human milk fatty acids, the findings were heterogeneous regarding the magnitude and directionality of associations for saturated fat, MUFAs, and PUFAs. For this reason, this element was rated 'grade not assignable.'
- **Directness** was graded as strong for the RCTs and moderate for the cross-sectional studies. As discussed previously, the primary objective of the RCTs aligned well with the systematic review question. For the cross-sectional studies, the study by Tian et al<sup>7</sup> seems to have been designed to assess the association between maternal dietary patterns during lactation and composition of fatty acids in human milk. However, it is less clear for Perrin et al<sup>6</sup> because the other article from this study (Pawlak et al<sup>5</sup>) reported that the power calculations were based on detecting differences in vitamin B<sub>12</sub> in human milk, suggesting that the Perrin et al<sup>6</sup> article could have been a secondary analysis.
- Precision was graded as limited for both RCTs and cross-sectional studies.
   The cross-sectional studies each had a reasonable sample size (n=274<sup>7</sup> and n=74<sup>6</sup>), although neither reported power calculations. The RCTs had small sample sizes (<20 participants). None of the studies unduly influenced the findings of this systematic review and removing one or more studies would not likely influence the conclusions.</p>
- Generalizability was graded as limited for both RCTs and cross-sectional studies. Although the RCTs were conducted in the U.S. and Canada, the studies reported minimal data on SES and race/ethnicity of the participants. The study by Perrin et al<sup>6</sup> was conducted in the U.S. and most of the participants

were highly educated White women. The study by Tian et al<sup>7</sup> was conducted in China, with 100 percent Han Chinese women from mid-to-upper SES. Based on these characteristics, it is unclear if the findings would apply to a diverse sample of U.S. mothers.

The bodies of evidence that assessed the relationship between 1) maternal dietary patterns and vitamin  $B_{12}$  in human milk, 2) maternal diets differing in macronutrient distributions and total protein concentration or human milk quantity were rated 'grade not assignable' primarily because only one study met the inclusion criteria.

Publication bias is always a concern; however, given that these studies were smaller in size and many of them had null findings, publication bias did not seem to be a serious concern in this evidence.

## **Research recommendations**

- Include diverse populations from the U.S. and elsewhere with varying age groups and different racial/ethnic and socioeconomic backgrounds.
- Foster collaborative efforts to score dietary patterns consistently, so that they can be compared and reproduced across studies.
- Assess other nutrients (particularly water- and fat-soluble vitamins), human milk oligosaccharides, and bioactive proteins in human milk.
- Use a consistent methodology for human milk collection and assessment.
- Include well-designed and sufficiently powered RCTs.
- Adjust for key confounding factors in observational studies including age, race/ethnicity, SES, anthropometry, smoking, parity, gestational age, and supplement intake during pregnancy and lactation.

## **Included articles**

- 1. Mohammad MA, Sunehag AL, Haymond MW. Effect of dietary macronutrient composition under moderate hypocaloric intake on maternal adaptation during lactation. *Am J Clin Nutr.* 2009;89(6):1821-1827. doi:10.3945/ajcn.2008.26877
- 2. Mohammad MA, Sunehag AL, Haymond MW. De novo synthesis of milk triglycerides in humans. *Am J Physiol Endocrinol Metab*. 2014;306(7):E838-847. doi:10.1152/ajpendo.00605.2013
- Nasser R, Stephen AM, Goh YK, Clandinin MT. The effect of a controlled manipulation of maternal dietary fat intake on medium and long chain fatty acids in human breast milk in Saskatoon, Canada. *Int Breastfeed J.* 2010;5:3. doi:10.1186/1746-4358-5-3
- 4. Yahvah KM, Brooker SL, Williams JE, Settles M, McGuire MA, McGuire MK. Elevated dairy fat intake in lactating women alters milk lipid and fatty acids without detectible changes in expression of genes related to lipid uptake or synthesis. *Nutr Res.* 2015;35(3):221-228. doi:10.1016/j.nutres.2015.01.004
- Pawlak R, Vos P, Shahab-Ferdows S, Hampel D, Allen LH, Perrin MT. Vitamin B-12 content in breast milk of vegan, vegetarian, and nonvegetarian lactating women in the United States. *Am J Clin Nutr.* 2018;108(3):525-531. doi:10.1093/ajcn/nqy104
- Perrin MT, Pawlak R, Dean LL, Christis A, Friend L. A cross-sectional study of fatty acids and brain-derived neurotrophic factor (BDNF) in human milk from lactating women following vegan, vegetarian, and omnivore diets. *Eur J Nutr.* 2019;58(6):2401-2410. doi:10.1007/s00394-018-1793-z
- 7. Tian HM, Wu YX, Lin YQ, et al. Dietary patterns affect maternal macronutrient intake levels and the fatty acid profile of breast milk in lactating Chinese mothers. *Nutrition*. 2019;58:83-88. doi:10.1016/j.nut.2018.06.009

Table 1. Description of evidence on the relationship between dietary patterns during lactation and human milk composition<sup>iv,v</sup>

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings				
Factor/Cluster Analysis								
Tian, 2019 <sup>7</sup> ; China Cross-sectional Study  Baseline N=287 Analytic N=274 (Attrition: 5%)  • Maternal age: Mean ~29.8y • Race/Ethnicity: 100% Chinese Han • SES: Family income (yuan/mo; n(%)), P=0.28: ○ <5000: 46 (16.8) ○ 5000-9999: 154 (56.2) ○ ≥10000: 74 (27.0)  • Anthropometry (median), P=0.89: ○ GWG: ~16.4 kg, P=0.78 ○ Prepregnancy BMI: ~20.6  • GA at birth: ~39.6wk • Supplement intake during lactation: None	Dietary Pattern(s): Pattern 1: Mushroom food and algae, Meat, Marine products (n=66) Pattern 2: Soybean products, Nuts, Dairy (n=63) Pattern 3: Fruit, Vegetables (n=73) Pattern 4: Grain/potato and beans, Eggs (n=72)  Dietary assessment methods: Data was collected using a 24-h dietary recall questionnaire and 176 item FFQ by a trained investigator to estimate dietary patterns. The foods were combined to make 10 groups: grains/potatoes and beans, soy bean products, mushrooms and algae, fruits, vegetables, nuts,	Significant: Human milk fatty acid proportions (%), Median (25th, 75th)  SAT, Kruksal-Wallis, P<0.001 Pattern 1: 40.38 (37.41, 44.25) Pattern 2: 42.92 (38.61, 49.62) Pattern 3: 39.10 (34.65, 45.04) Pattern 4: 42.92 (40.31, 49.93)  PUFAS, Kruksal-Wallis, P=0.025 Pattern 1: 24.49 (21.73, 28.43) Pattern 2: 22.09 (19.92, 27.08) Pattern 3: 24.63 (20.37, 29.17) Pattern 4: 22.77 (19.49, 26.38)	Key confounders accounted for: Race/ethnicity, Anthropometry, GA  Limitations: • Time of exposure measurement relative to outcome is not clear • Lactation stage varies (22 d to 6 mo) • Single measurement of exposure and outcome • Power calculation NR	Maternal dietary patterns were associated with human milk saturated fatty acids, PUFAs, and n-6 PUFA proportions, but not with MUFAs, n-3 PUFAs, or n-6/n-3 PUFA proportions.				

iv ± indicates values of Mean± SD unless otherwise noted

<sup>&</sup>lt;sup>v</sup> AA: arachidonic acid, ALA: alpha-linolenic acid, ANOVA: analysis of variance, BMI: body mass index, d: day(s) DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid, FFQ: food frequency questionnaire, GA: gestational age, GWG: gestational weight gain, h: hour, IQR: interquartile range, kg: kilogram(s), LA: linoleic acid, mo: month(s), MUFA: monounsaturated fatty acid, n-#: omega-#, NR: not reported, PUFA: polyunsaturated fatty acid, SAT: saturated fat, SES: socioeconomic status, wk: week(s), y: year(s)

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	meat, eggs, marine products, and dairy products. These groups were assigned to 1 of 4 dietary patterns using a rotated component matrix.  Outcomes: Human milk composition:	<ul> <li>n-6 PUFAs, Kruksal-Wallis, P=0.038</li> <li>Pattern 1: 20.71 (18.11, 23.27)</li> <li>Pattern 2: 18.24 (16.41, 22.71)</li> <li>Pattern 3: 20.11 (17.33, 24.22)</li> </ul>		
	Macronutrients: Fatty acid once during 22d to 6mo postpartum	o Pattern 4: 18.49 (16.11, 21.89)		
	Outcome assessment methods: After discarding the first few drops, a total of 30 mL of milk was collected. The profile of fatty acid in human milk was detected by capillary gas chromatography and calculated with fatty acid methylesters (FAME) using the internal standard method.	Non-significant: Human milk fatty acid proportions (%), Median (25th, 75th)  • MUFAs, Kruksal-Wallis, P=0.053  ○ Pattern 1: 34.40 (31.20, 36.84)  ○ Pattern 2: 33.53 (29.91, 36.42)  ○ Pattern 3: 34.85 (31.39, 39.58)  ○ Pattern 4: 33.45 (29.09, 35.39)		
		<ul> <li>n-3 PUFAs, Kruksal-Wallis, P=0.29</li> <li>Pattern 1: 3.96 (2.70, 5.01)</li> <li>Pattern 2: 3.55 (2.98, 4.46)</li> <li>Pattern 3: 3.56 (2.32, 4.98)</li> <li>Pattern 4: 3.86 (3.09, 4.56)</li> </ul>		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		<ul> <li>n-6/n-3 PUFAs, Kruksal-Wallis, P=0.34</li> <li>Pattern 1: 4.83 (3.80, 7.32)</li> <li>Pattern 2: 4.76 (4.14, 6.30)</li> <li>Pattern 3: 5.34 (3.74, 9.39)</li> <li>Pattern 4: 4.69 (3.85, 5.74)</li> </ul>		
Other Dietary Pattern Analy	rsis			
Pawlak, 2018 <sup>5</sup> ; U.S. Cross-sectional Study  Baseline N=74 Analytic N=74 (Attrition: 0%)  • Maternal age: Mean ~32y • Race/Ethnicity:	Dietary Pattern(s):  Vegan: Never consumed meat and never or rarely consumed other animal products (1 time/mo) (n=26)  Vegetarian: Never consumed meat and regularly consumed other animal products (n=22)  Nonvegetarian: Consumed meat sometimes or often (n=26)  Dietary assessment methods: Diet survey; Unclear timing and validation  Outcomes: Human milk composition: Vitamin B <sub>12</sub> assessment once at ~38.8wk postpartum	Significant: None  Non-significant: Human milk B <sub>12</sub> (pmol/L), Median (quartile 1, quartile 3): Unadjusted: ANOVA P=0.89, Kruskal-Wallis P=0.94 • Vegan: 558 (331, 759); • Vegetarian: 509 (368, 765 pmol/L); • Nonvegetarian: 444 (355, 777) Adjusted (BMI, lactation stage) ANOVA: P=0.89  Human milk B <sub>12</sub> >1122 pmol/L (%), P=0.72 • Vegan: 15.4 • Vegetarian: 9.1 • Nonvegetarian: 7.7	Key confounders accounted for: Anthropometry  Limitations: Baseline differences in maternal BMI, lactation stage and supplement use Majority of the participants (77.4%) reported using vitamin B <sub>12</sub> supplements Only one time point of exposure and outcome measurement No validation of exposure assessment Unclear why 61 eligible participants did not respond and whether their characteristics were different from the participants that enrolled	There was no significant difference between vitamin B <sub>12</sub> levels in human milk between 3 dietary patterns (vegan, vegetarian and nonvegetarian)

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
<ul> <li>Vegetarian: 23.9±3.8</li> <li>Nonveg: 25.8±4.5</li> <li>Parity: ~1.9</li> <li>Supplement intake during lactation, n (%)</li> <li>B<sub>12</sub>, P=0.001: Vegan: 12 (46.2), Veg: 6 (27.3), Nonveg: 1 (3.9)</li> <li>B-complex, P=0.771: Vegan: 2 (7.7), Veg: 0 (0), Nonveg: 1 (3.9)</li> <li>Multivitamin, P=0.083: Vegan: 4 (15.4), Veg: 0 (0), Nonveg: 5 (19.2)</li> <li>Prenatal, P=0.92: Vegan: 14 (53.9), Veg: 13 (59.1), Nonveg: 14 (53.8)</li> <li>Any B-vitamin, P=0.09: Vegan: 24 (92.3), Veg: 16 (72.7), Nonveg: 18 (69.2)</li> </ul>	<ul> <li>Vegan: 36.6± 27.7wk</li> <li>Vegetarian: 54.6± 46.0wk</li> <li>Nonvegetarian: 27.5± 19.8wk         <ul> <li>Vegetarian vs</li> <li>Nonvegetarian, P&lt;0.05</li> </ul> </li> <li>Outcome assessment methods:         <ul> <li>Completely express the content of 1 breast in the morning (≥ 2h since the previous feeding).</li> <li>Competitive chemiluminescent enzyme immunoassay. Milk samples with vitamin B<sub>12</sub> concentrations above upper detection limit assigned max value (1122 pmol/L) and flagged.</li> </ul> </li> </ul>	Human milk B <sub>12</sub> <310 pmol/L (%), P=1.00 • Vegan: 19.2 • Vegetarian: 18.2 • Nonvegetarian: 15.4	Stage of lactation was significantly different between the three groups	
Perrin, 2019 <sup>6</sup> ; U.S. Cross-sectional Study	<ul><li>Dietary Pattern(s):</li><li>Vegan: Never consumed meat and never or rarely</li></ul>	Significant: Data are median (IQR); Significance P≤0.001	Key confounders accounted for: None	Human milk from vegans had significantly higher unsaturated fat and total n-3
Baseline N=74	consumed other animal	% SAT, ANOVA, P<0.001	Limitations:	PUFAs, and lower saturated
Analytic N=74	products (1 time/mo)	<ul><li>Vegan: 33.1 (6.2);</li></ul>	<ul> <li>Baseline differences in</li> </ul>	fatty acids, trans fats, and n
(Attrition: 0%)	(n=26) • Vegetarian: Never	<ul> <li>Vegetarian: 40.0 (8.6);</li> <li>Negropotarian: 42.3 (8.4)</li> </ul>	maternal BMI, lactation stage and supplement use	6/n-3 PUFA ratio than their vegetarian and
Maternal age: Mean	consumed meat and	<ul> <li>Nonvegetarian: 42.3 (8.4)</li> </ul>	<ul> <li>Only one time point of</li> </ul>	nonvegetarian counterparts
~31.95y	regularly consumed other	% C15:0, Kruskal-Wallis,	exposure and outcome	DHA concentrations in
Race/Ethnicity:	animal products (n=22)	P<0.001	measurement	human milk were low
o White=85.1%	Nonvegetarian:	<ul> <li>Vegan: 0.06 (0.08)</li> </ul>	<ul> <li>No validation of exposure</li> </ul>	regardless of maternal
Mixed/Other-0 40/	Canaumad moat	) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) (	oooooomont '	dietary nattern, and were

• Vegetarian: 0.24 (0.20)

• Nonvegetarian: 0.26

(0.16)

assessment

o Mixed/Other=9.4%

Hispanic=4%Asian=1.4%

Consumed meat

sometimes or often (n=26)

dietary pattern, and were

reflective of low seafood

intake and supplement use.

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
<ul> <li>Black=0%</li> <li>SES: Education:         <ul> <li>HS/GED/other: 2.7%</li> <li>Some college/ technical: 16.2%</li> <li>4y college: 37.8%</li> <li>Graduate: 43.2%</li> </ul> </li> <li>Anthropometry: BMI (mean± SD), P=0.02:             <ul> <li>Vegan: 22.8±3.1</li> <li>Vegetarian: 23.9±3.8</li> <li>Nonveg: 25.8±4.5</li> </ul> </li> <li>Parity: ~1.9</li> <li>Supplement intake during lactation, n (%):                  <ul> <li>B12, P=0.001: Vegan: 12 (46.2), Veg: 6 (27.3), Nonveg: 1 (3.9)</li> <li>B-complex, P=0.771: Vegan: 2 (7.7), Veg: 0 (0), Nonveg: 1 (3.9)</li> <li>Multivitamin, P=0.083: Vegan: 4 (15.4), Veg: 0 (0), Nonveg: 5 (19.2)</li> <li>Prenatal, P=0.92: Vegan: 14 (53.9), Veg: 13 (59.1), Nonveg: 14 (53.8)</li> <li>Any B-vitamin, P=0.09: Vegan: 24 (92.3), Veg: 16 (72.7), Nonveg: 18 (69.2)</li> </ul> </li> </ul>	Dietary assessment methods: Diet survey; Unclear timing and validation  Outcomes: Human milk composition: Fatty acid once at ~38.8wk postpartum • Vegan: 36.6± 27.7wk • Vegetarian: 54.6± 46.0wk • Nonvegetarian: 27.5± 19.8wk ○ Vegetarian vs Nonvegetarian, P<0.05  Outcome assessment methods: Completely express the content of 1 breast in the morning (≥ 2h since the previous feeding). Total fat measured by creamatocrit. The fatty acid present in the samples measured as fatty acid methyl esters according to Bannon et al method	<ul> <li>% C16:0, ANOVA, P&lt;0.001</li> <li>Vegan: 13.32 (2.49)</li> <li>Vegetarian: 18.57 (5.22)</li> <li>Nonvegetarian: 20.02 (4.43)</li> <li>% C17:0, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 0.12 (0.02)</li> <li>Vegetarian: 0.22 (0.11)</li> <li>Nonvegetarian: 0.26 (0.07)</li> <li>% C18:0, ANOVA, P&lt;0.001</li> <li>Vegan: 3.98 (1.27)</li> <li>Vegetarian: 5.85 (2.52)</li> <li>Nonvegetarian: 6.12 (1.72)</li> <li>% Unsaturated fat, ANOVA, P&lt;0.001</li> <li>Vegan: 66.0 (6.5)</li> <li>Vegetarian: 57.8 (9.8)</li> <li>Nonvegetarian: 56.2 (8.5)</li> <li>% Total n-3 PUFAs, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 2.29 (0.77)</li> <li>Vegetarian: 1.55 (0.56)</li> <li>Nonvegetarian: 1.46 (0.94)</li> <li>% ALA (C18:3 cis), Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 2.09 (0.75)</li> <li>Vegetarian: 1.40 (0.70)</li> </ul>	<ul> <li>Dietary patterns not fully defined using a priori/ posteriori methods</li> <li>Unclear why 61 eligible participants did not respond and whether their characteristics were different from the participants that enrolled</li> <li>Power calculation was based on detecting differences in milk B<sub>12</sub></li> </ul>	

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		<ul> <li>Nonvegetarian: 1.19 (0.80)</li> </ul>		
		<ul> <li>% C18:3 cis, γ, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 0.0 (0.0)</li> <li>Vegetarian: 0.0 (0.15)</li> <li>Nonvegetarian; 0.08 (0.19)</li> </ul>		
		LA:ALA, Kruskal-Wallis, P<0.001 • Vegan: 9.3 (2.1) • Vegetarian: 12.2 (4.9) • Nonvegetarian: 12.7 (6.2)		
		n-6: n-3 PUFAs, Kruskal-Wallis, P<0.001  Vegan: 8.8 (2.4)  Vegetarian: 11.4 (3.7)  Nonvegetarian: 11.2 (3.8)		
		<ul> <li>% C14:1 cis, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 0.00 (0.07)</li> <li>Vegetarian: 0.20 (0.13)</li> <li>Nonvegetarian: 0.23 (0.15)</li> </ul>		
		<ul> <li>% C16:1 cis 9, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 1.01 (0.89)</li> <li>Vegetarian: 1.44 (0.86)</li> <li>Nonvegetarian: 2.04 (0.63)</li> </ul>		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		<ul> <li>% C17:1 cis, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 0.03 (0.08)</li> <li>Vegetarian: 0.12 (0.09)</li> <li>Nonvegetarian: 0.16 (0.06)</li> </ul>		
		<ul> <li>% C18:1 cis, ANOVA,</li> <li>P&lt;0.001</li> <li>Vegan: 39.86 (7.56)</li> <li>Vegetarian: 35.09 (7.96)</li> <li>Nonvegetarian: 33.09 (8.50)</li> </ul>		
		<ul> <li>% Total trans fat, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 0.44 (0.19)</li> <li>Vegetarian: 0.66 (0.71)</li> <li>Nonvegetarian: 1.09 (0.55)</li> </ul>		
		<ul> <li>% C18:1 trans, Kruskal-Wallis, P&lt;0.001</li> <li>Vegan: 0.00 (0.07)</li> <li>Vegetarian: 0.14 (0.61)</li> <li>Nonvegetarian: 0.62 (0.45)</li> </ul>		
		Non-significant: Data are median (IQR); Significance P≤0.001 Total fat (g/dL), Kruskal- Wallis, P=0.041  • Vegan: 3.0 (1.7)  • Vegetarian: 4.0 (2.9)  • Nonvegetarian: 4.0 (2.9)		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		% C8:0, ANOVA, P=0.052		
		<ul><li>Vegan: 0.21 (0.13)</li></ul>		
		<ul> <li>Vegetarian: 0.18 (0.15)</li> </ul>		
		<ul> <li>Nonvegetarian: 0.17 (0.18)</li> </ul>		
		% C10:0, Kruskal-Wallis, P=0.332		
		<ul> <li>Vegan: 1.46 (0.71)</li> </ul>		
		<ul> <li>Vegetarian: 1.50 (0.74)</li> </ul>		
		Nonvegetarian: 1.65		
		(0.43)		
		% C12:0, Kruskal-Wallis,		
		P=0.186		
		• Vegan: 7.12 (3.63)		
		<ul><li>Vegetarian: 5.88 (2.01)</li><li>Nonvegetarian: 6.22</li></ul>		
		(3.07)		
		% C14:0, Kruskal-Wallis,		
		P=0.571		
		• Vegan: 5.55 (3.89)		
		<ul><li>Vegetarian: 6.81 (3.06)</li><li>Nonvegetarian: 6.56</li></ul>		
		(3.36)		
		% C20:0, Kruskal-Wallis,		
		P=0.002		
		<ul> <li>Vegan: 0.16 (0.14)</li> <li>Vegatorian: 0.20 (0.16)</li> </ul>		
		<ul><li>Vegetarian: 0.20 (0.16)</li><li>Nonvegetarian: 0.09</li></ul>		
		(0.15)		
		% C22:0, Kruskal-Wallis,		
		P=0.015		
		• Vegan: 0.06 (0.09)		
		<ul> <li>Vegetarian: 0.05 (0.08)</li> </ul>		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		<ul> <li>Nonvegetarian: 0.00         <ul> <li>(0.04)</li> </ul> </li> </ul>		
		<ul> <li>% C24:0, Kruskal-Wallis,</li> <li>P=0.765</li> <li>Vegan: 0.00 (0.07)</li> <li>Vegetarian: 0.06 (0.08)</li> <li>Nonvegetarian: 0.00 (0.08)</li> </ul>		
		<ul> <li>% EPA (C20:5 cis), Kruskal-Wallis, P=0.057</li> <li>Vegan: 0.0 (0.05)</li> <li>Vegetarian: 0.0 (0.05)</li> <li>Nonvegetarian: 0.04 (0.18)</li> </ul>		
		<ul> <li>% DHA (C22:6 cis),</li> <li>Kruskal-Wallis, P=0.543</li> <li>Vegan: 0.14 (0.09)</li> <li>Vegetarian: 0.17 (0.14)</li> <li>Nonvegetarian: 0.18 (0.18)</li> </ul>		
		<ul> <li>% Total n-6 PUFAs,</li> <li>ANOVA, P=0.492</li> <li>Vegan: 19.65 (2.88)</li> <li>Vegetarian: 18.69 (6.76)</li> <li>Nonvegetarian: 17.11 (6.39)</li> </ul>		
		<ul> <li>% LA (C18:2 cis), ANOVA,</li> <li>P=0.366</li> <li>Vegan: 18.86 (2.29)</li> <li>Vegetarian: 17.98 (6.91)</li> <li>Nonvegetarian: 16.28 (6.40)</li> </ul>		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		<ul> <li>% C20:3 cis, Kruskal-Wallis,</li> <li>P=0.106</li> <li>Vegan: 0.27 (0.09)</li> <li>Vegetarian: 0.34 (0.11)</li> <li>Nonvegetarian: 0.31 (0.13)</li> </ul>		
		<ul> <li>% AA (C20:4), ANOVA,</li> <li>P=0.014</li> <li>Vegan: 0.38 (0.21)</li> <li>Vegetarian: 0.38 (0.13)</li> <li>Nonvegetarian: 0.45 (0.16)</li> </ul>		
		<ul> <li>% C15:1 cis, Kruskal-Wallis,</li> <li>P=0.002</li> <li>Vegan: 0.00 (0.00)</li> <li>Vegetarian: 0.00 (0.05)</li> <li>Nonvegetarian 0.00 (0.04)</li> </ul>		
		<ul> <li>% C20:1 cis, Kruskal-Wallis, P=0.003</li> <li>Vegan: 0.38 (0.16)</li> <li>Vegetarian: 0.33 (0.10)</li> <li>Nonvegetarian: 0.29 (0.12)</li> </ul>		
		<ul> <li>% C20:2 cis, Kruskal-Wallis, P=0.873</li> <li>Vegan: 0.26 (0.15)</li> <li>Vegetarian: 0.26 (0.08)</li> <li>Nonvegetarian: 0.27 (0.11) (P=0.873)</li> </ul>		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		% C22:1 cis, Kruskal-Wallis,		
		P=0.278		
		<ul><li>Vegan: 0.00 (0.09)</li><li>Vegetarian: 0.05 (0.07)</li></ul>		
		<ul><li>Nonvegetarian: 0.00</li></ul>		
		(0.05) (P=0.278)		
		% C24:1 cis, Kruskal-Wallis,		
		P=0.430		
		• Vegan: 0.00 (0.01)		
		• Vegetarian: 0.00 (0.03)		
		• Nonvegetarian: 0.00 (0.0)		
		% C14:1 trans, Kruskal-		
		Wallis, P=0.108		
		<ul> <li>Vegan: 0.00 (0.00)</li> </ul>		
		• Vegetarian: 0.00 (0.03)		
		Nonvegetarian: 0.00     (0.00)		
		(0.00)		
		% C16:1 trans, ANOVA,		
		P=0.863		
		<ul> <li>Vegan: 0.36 (0.17)</li> </ul>		
		• Vegetarian: 0.34 (0.10)		
		<ul> <li>Nonvegetarian: 0.36</li> </ul>		
		(0.10)		
		% C18:2 trans, Kruskal-		
		Wallis, P=0.021		
		• Vegan: 0.00 (0.07)		
		• Vegetarian: 0.14 (0.34)		
		<ul> <li>Nonvegetarian: 0.15 (0.29)</li> </ul>		
		Medium chain (%), Kruskal-		
		Wallis, P=0.897		
		<ul> <li>Vegan: 14.9 (6.3)</li> </ul>		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		<ul> <li>Vegetarian: 14.6 (5.6)</li> </ul>		
		<ul> <li>Nonvegetarian: 14.9 (6.7)</li> </ul>		
		Long chain (%), Kruskal-		
		Wallis, 0.906		
		<ul> <li>Vegan: 85.1 (6.9)</li> </ul>		
		<ul> <li>Vegetarian: 85.4 (5.9)</li> </ul>		
		<ul> <li>Nonvegetarian: 85.6 (6.7)</li> </ul>		

Table 2. Description of evidence on the relationship between diets based on macronutrient distributions during lactation and human milk composition and quantity<sup>vi,vii</sup>

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
Randomized Controlled Tri	als			
Mohammad, 2014 <sup>2</sup> ; U.S. RCT: Crossover	Macronutrient Proportion(s):	Significant: All values are Mean g/L Total fatty acid	Key confounders accounted for: None	Total milk fat was significantly higher during H-FAT diet, when compared
Baseline N=7 Analytic N=7 (Attrition: 0%)  • Maternal age (Mean±SEM): 28.5± 1.2y • Race/Ethnicity:	'H-FAT': 30% CHO, 55% FAT, 15% PRO     'H-CHO': 60% CHO, 25% FAT, 15% PRO for 8d on each diet with 1-2wk washout during 6-14wk postpartum  Dietary assessment methods: Diets were created to achieve the designed macronutrient composition. Total energy intake and distribution of energy from CHO, FAT, and PRO were analyzed by using NDSR.  Outcomes: Human milk composition: Fatty acids	<ul> <li>Feeding: H-CHO: 42.239, H-FAT: 46.893, P&lt;0.05</li> <li>C4:0</li> <li>Fasting: H-CHO: 0.102, H-FAT: 0.071, P&lt;0.05</li> <li>Feeding: H-CHO: 0.148, H-FAT: 0.087, P&lt;0.05</li> <li>C6:0</li> <li>Fasting: H-CHO: 0.202, H-FAT: 0.131, P&lt;0.01</li> <li>Feeding: H-CHO: 0.333, H-FAT: 0.183, P&lt;0.05</li> <li>C8:0</li> <li>Fasting: H-CHO: 0.357, H-FAT: 0.246, P&lt;0.01</li> <li>Feeding: H-CHO: 0.530, H-FAT: 0.381, P&lt;0.01</li> </ul>	<ul> <li>Limitations:</li> <li>Unclear baseline imbalances</li> <li>No adjustment for multiple comparisons</li> <li>No information on randomization, blinding, or carry-over effects</li> <li>Power calculation NR</li> </ul>	to H-CHO diet. Total MUFAs and PUFAs in human milk was significantly higher during H-FAT diet vs H-CHO diet. These findings were relevant only during (maternal) fed state.

vi ± indicates values of Mean± SD unless otherwise noted

vii AA: arachidonic acid, ALA: alpha-linolenic acid, BMI: body mass index, CHO: carbohydrate, CLA: conjugated linoleic acid, d: day(s), DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid, FA: fatty acid, GA: gestational age, GC-MS: gas chromatography-mass spectrometry, h: hour(s), LA: linoleic acid, mo: month(s), MUFA: monounsaturated fatty acid, n-#: omega-#, NDSR: Nutrition Data System for Research, NR: not reported, NS: non-significant, PUFA: polyunsaturated fatty acid, PRO: protein, RCT: randomized controlled trial, SAT: saturated fat, SEM: standard error of the mean, wk: week(s), y: year(s)

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	Every 3h collected during the 3d inpatient stay.  Outcome assessment methods:  During human milk feeding, once every 3h, 2.5 mL of milk from each breast was collected at the beginning, middle and after the feeding (total of 15 mL). Milk samples for each collection time were pooled for analyses. After human milk feeding, mothers were asked to empty the breast and milk was weighed. The 13C enrichment and quantification of fatty acid in milk performed on samples using the PFBBr derivatization and GC-MS negative chemical ionization.	C10:0 Fasting: H-CHO: 1.313, H-FAT: 1.112, P<0.05 Feeding: H-CHO: 1.920, H-FAT: 1.547, P<0.05  C12:0: Feeding: H-CHO: 3.569, H-FAT: 3.078, P<0.05  C14:0: Fasting: H-CHO: 2.632, H-FAT: 2.320, P<0.01 Feeding: H-CHO: 3.915, H-FAT: 3.427, P<0.01  Total C2:C14: Fasting: H-CHO: 7.230, H-FAT: 6.269, P<0.01 Feeding: H-CHO: 10.423, H-FAT: 8.712, P<0.01  C16:0: Feeding: H-CHO: 4.846, H-FAT: 5.620, P<0.05  C18:0: Feeding: H-CHO: 2.944, H-FAT: 4.034, P<0.01  C18:1: Feeding: H-CHO: 10.110, H-FAT: 13.230, P<0.01		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		• Feeding: H-CHO: 13.371, H-FAT: 16.008, P<0.01		•
		C18:2: • Feeding: H-CHO: 6.317, H-FAT: 7.595, P<0.01		
		C18:3: • Feeding: H-CHO: 1.268, H-FAT: 1.836, P<0.01		
		C20:2: • Fasting: H-CHO: 0.598, H-FAT: 0.439, P<0.05		
		C20:3: • Fasting: H-CHO: 0.616, H-FAT: 0.372, P<0.05		
		C20:4: • Fasting: H-CHO: 1.120, H-FAT: 0.820, P<0.05		
		C20:5: • Fasting: H-CHO: 0.106, H-FAT: 0.024, P<0.05		
		C22:6: • Fasting: H-CHO: 0.664, H-FAT: 0.408, P<0.05		
		Total PUFAs: • Feeding: H-CHO: 10.655, H-FAT: 12.519, P<0.05		
		% Total C2:C14:		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	•	<ul> <li>Fasting: H-CHO: 17.096, H-FAT: 15.054, P&lt;0.05</li> <li>Feeding: H-CHO: 24.699, H-FAT: 18.613, P&lt;0.01</li> </ul>	•	-
		% Total SAT: • Feeding: H-CHO: 43.139, H-FAT: 39.142, P<0.05		
		<ul> <li>% Total MUFAs:</li> <li>Fasting: H-CHO: 35.459, H-FAT: 38.962, P&lt;0.05</li> <li>Feeding: H-CHO: 31.753, H-FAT: 34.289, P&lt;0.05</li> </ul>		
		Non-significant: All values are Mean g/L Total FAs • Fasting: H-CHO: 41.908, H-FAT: 40.833, P=NS		
		C2:0 • Fasting: H-CHO: 0.007, H-FAT: 0.008, P=NS • Feeding: H-CHO: 0.008, H-FAT: 0.009, P=NS		
		C12:0: • Fasting: H-CHO: 2.618, H-FAT: 2.383, P=NS		
		C16:0: • Fasting: H-CHO: 5.326, H-FAT: 5.456, P=NS		
		C18:0:		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	_	• Fasting: H-CHO: 3.157, H-FAT: 3.308, P=NS		-
		Total SAT: • Fasting: H-CHO: 15.713, H-FAT: 15.033, P=NS • Feeding: H-CHO: 18.212, H-FAT: 18.366, P=NS		
		C16:1: • Fasting: H-CHO: 2.040, H-FAT: 2.125, P=NS • Feeding: H-CHO: 2.143, H-FAT: 1.760, P=NS		
		C18:1: • Fasting: H-CHO: 11.408, H-FAT: 12.748, P=NS		
		C20:1: • Fasting: H-CHO: 1.303, H-FAT: 0.909, P=NS • Feeding: H-CHO: 1.118, H-FAT: 1.018, P=NS		
		Total MUFAs: • Fasting: H-CHO: 14.751, H-FAT: 15.783, P=NS		
		C18:2: • Fasting: H-CHO: 6.678, H-FAT: 6.471, P=NS		
		C18:3: • Fasting: H-CHO: 1.403, H-FAT: 1.335, P=NS		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	_	C20:2:	-	-
		<ul> <li>Feeding: H-CHO: 0.493,</li> </ul>		
		H-FAT: 0.532, P=NS		
		C20:3:		
		<ul> <li>Feeding: H-CHO: 0.657,</li> </ul>		
		H-FAT: 0.563, P=NS		
		C20:4:		
		<ul> <li>Feeding: H-CHO: 1.020,</li> </ul>		
		H-FAT: 1.173, P=NS		
		C20:5:		
		<ul> <li>Feeding: H-CHO: 0.083,</li> </ul>		
		H-FAT: 0.056, P=NS		
		C22:5:		
		<ul> <li>Fasting: H-CHO: 0.261,</li> </ul>		
		H-FAT: 0.148, P=NS		
		<ul> <li>Feeding: H-CHO: 0.234,</li> </ul>		
		H-FAT: 0.229, P=NS		
		C22:6:		
		<ul> <li>Feeding: H-CHO: 0.582,</li> </ul>		
		H-FAT: 0.535, P=NS		
		Total PUFAs:		
		<ul> <li>Fasting: H-CHO: 11.445,</li> </ul>		
		H-FAT: 10.017, P=NS		
		% Total SAT:		
		<ul> <li>Fasting: H-CHO: 37.198,</li> </ul>		
		H-FAT: 36.230, P=NS		
		% Total PUFAs:		
		• Fasting: H-CHO: 27.342,		
		H-FAT: 24.809, P=NS		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	•	• Feeding: H-CHO: 25.108, H-FAT: 26.569, P=NS		
Mohammad, 2009¹; U.S. RCT: Crossover  Baseline N=7 Analytic N=7 (Attrition: 0%)  • Maternal age (Mean±SEM): 28.5± 1.2y • Race/Ethnicity:	Macronutrient Proportion(s):  • 'H-FAT': 30% CHO, 55% FAT, 15% PRO • 'H-CHO': 60% CHO, 25% FAT, 15% PRO for 8d on each diet with 1- 2wk washout during 6-14wk postpartum  Dietary assessment methods: Crossover design: Intervention 1 (8d), Washout (1-2wk), Intervention 2 (8d). Diets created to achieve designed macronutrient composition. Total energy intake and distribution of energy from CHO, FAT, and PRO analyzed using NDSR. During each study period, women consumed study- provided diet for 4d in their homes, and then consumed the same diet for 4d and 3 nights in the research center.  Outcomes: Human milk composition: Protein, Fat	Significant: Composition (Mean± SEM), Paired t-test Fat (g/dL), P<0.05 • H-CHO: 4.3± 0.3 • H-FAT: 4.8± 0.3  Fat (g/d), P<0.05 • H-CHO: 34± 2 • H-FAT: 39± 2  Non-significant: Composition (Mean± SEM), Paired t-test Protein (g/dL), P=NS • H-CHO: 1.8± 0.1 • H-FAT: 1.9± 0.1  Protein (g/d), P=NS • H-CHO: 15± 0.9 • H-FAT: 16± 0.8  Milk volume (mL/d, Mean± SEM), Paired t-test, P=NS • H-CHO: 829± 41 • H-FAT: 821± 33	Key confounders accounted for: None  Limitations:  No adjustment for multiple comparisons Unclear baseline imbalances No information on randomization, blinding, or carry-over effects Power calculation NR	Consuming a reduced-calorie H-FAT diet compared to an isocaloric, isonitrogenous H-CHO increased total fat milk concentration, but did not affect milk protein concentrations or volume.

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	Every 3h collected during the 3d inpatient stay, which occurred twice during 6-14wk postpartum			
	Human milk quantity Every 3h collected during the 3d inpatient stay, which occurred twice during 6- 14wk postpartum			
	Outcome assessment methods:			
	During human milk feeding, once every 3 h, 2.5 mL of milk from each breast was collected at the beginning, middle and after the feeding (total of 15 mL). Milk samples for each collection time were pooled for analyses. After human milk feeding, mothers were asked to empty the breast and the milk was weighed. Total lipid content was quantified gravimetrically; protein was measured by using a bicinchoninic acid protein assay kit.  The daily intake of the infants was determined on the basis of the milk volume consumed and the energy content of the milk.			

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
Nasser, 2010 <sup>3</sup> ; Canada RCT: Crossover	Macronutrient Proportion(s):	Significant: Human milk fat composition (g/100 g total fatty acids),	Key confounders accounted for: Smoking Status, GA	No significant difference in human milk concentrations of total saturated, MUFAs,
Baseline N=14	• HF: 40.3% FAT, 14.4%	Mean± SEM	<b>5</b>	and PUFAs during high fat
Analytic N=14	PRO, 45.3% CHO	Capria asid (C10:0) D	Limitations:	or low fat diet.
(Attrition: 0%)	<ul> <li>LF: 17.6% FAT, 14.4%</li> <li>PRO, 68% CHO</li> </ul>	Capric acid (C10:0), P= 0.01	<ul> <li>No adjustment for multiple comparisons</li> </ul>	
<ul> <li>Maternal age: 31.6 y</li> </ul>	for 4d on each diet with 3d	• LF: 0.87± 0.04	Short study duration	
(range 24-37)	washout during 2-6mo	• HF: 0.68± 0.03	Power calculation NR	
Anthropometry: BMI: 26	postpartum			
Smoking status: 0%	Dietery coccement	Lauric acid (C12:0), P=0.01		
<ul> <li>Parity: 6 primiparae, 8 multiparae</li> </ul>	Dietary assessment methods:	• LF: 5.38± 1.16		
GA at birth: 100% Full-	Women randomly assigned	• HF: 3.98± 0.37		
term	to receive each dietary			
Infant age (Mean± SEM):	intervention (low fat and	Total medium chain fatty		
2.8± 0.9mo (range 2-6mo)	high fat), with equal	acids, P=0.01 • LF: 13.56± 0.66		
	numbers of participants for each order of treatment.	• HF: 11.42± 0.86		
	Women were provided with	• TH : 11.42± 0.00		
	prepared meals and snacks	Stearic acid (C18:0), P=0.01		
	meeting their daily energy	• LF: 5.00± 0.11		
	requirement, as determined	• HF: 6.08± 0.14		
	by the dietary assessment prior to the period of diet			
	control.	Arichidic acid (C20:0),		
	control.	P=0.02		
	Outcomes:	• LF: 0.08± 0.07		
	Human milk composition:	• HF: 0.12± 0.01		
	fatty acids	D   ''   '   '   '   '   '   '   '   '		
	Once during 2-6mo postpartum	Palmitoleic acid (C16:1n-7),		
	postpartam	P=0.046 • LF: 1.95± 0.29		
	Outcome assessment	• HF: 1.31± 0.23		
	methods:	1.012 0.20		
	Each mother espressed 20-	Eicosenoic acid (C20:1n-9),		
	50mL of human milk	P=0.01		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	between 1-2pm. Milk was pumped from a breast after the baby latched and fed for	<ul><li>LF: 0.27± 0.02</li><li>HF: 0.38± 0.02</li></ul>	-	
	2-5 minutes. Average fat content was assessed in the hind milk	ALA (C18:3n-3), P=0.01 • LF: 1.22± 0.04 • HF:1.69± 0.06		
	extracted for medium and long chain fatty acids using a modified Folch procedure.	γ-linoenic acid (C18:3n-6), P=0.02 • LF: 0.12± 0.01 • HF: 0.09± 0.01		
		Dihomo-y-linolenic acid (C20:3n-6), P=0.03 • LF: 0.27± 0.02 • HF: 0.24± 0.02		
		AA (C20:4n-6), P=0.02 • LF: 0.34± 0.01 • HF: 0.30± 0.02		
		Non-significant: Human milk fat composition (g/100 g total fatty acids), Mean± SEM		
		Total SAT, P=0.46 • LF: 41.1± 0.82 • HF: 40.40± 0.85		
		Caprylic acid (C8:0) • LF: Trace • HF: Trace		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	-	Myristic acid (C14:0),		-
		P=0.07		
		• LF: 7.31± 0.35		
		• HF: 6.76± 0.48		
		Palmitic acid (C16:0),		
		P=0.43		
		• LF: 22.70± 0.45		
		• HF: 23.43± 0.24		
		Total MUFAs, P=0.10		
		• LF: 38.70± 0.80		
		• HF: 39.90± 0.65		
		Myristoleic acid (C14:1n-5),		
		P=0.27		
		• LF: 0.35± 0.01		
		• HF: 0.41± 0.05		
		Oleic acid (C18:1n-9),		
		P=0.08		
		• LF: 36.16± 0.86		
		• HF: 37.81± 0.67		
		Total PUFAs, P=0.54		
		• LF: 16.90± 0.66		
		• HF: 16.40± 0.48		
		LA (C18:2n-6), P=0.27		
		• LF: 14.65± 0.62		
		• HF: 13.82± 0.45		
		Eicosadienoic acid (C20:2n-		
		6), P=0.51		
		• LF: 0.19± 0.02		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	-	• HF: 0.18± 0.01		-
		EPA (C20:5n-3)		
		LF: Trace		
		HF: Trace		
		Docasapentaenoic acid		
		(C22:5n-3)		
		LF: Trace		
		HF: Trace		
		DHA (C22:6n-3), P= 0.77		
		• LF: 0.12± 0.02		
		• HF: 0.14± 0.04		
Yahvah, 2015 <sup>4</sup> ; U.S. RCT: Crossover	Macronutrient Proportion(s):	Significant: Mean± SEM, Paired t-tests: Total lipids (g/100 g milk),	Key confounders accounted for: None	Consuming a diet rich in full-fat versus low-fat dairy
Baseline N=16	<ul> <li>Low-fat dairy (LFD): ~24%</li> </ul>	P<0.05		products during lactation was associated with
Analytic N=15	FAT, ~20% PRO, ~57%	• FFD: 3.35± 0.28	Limitations:	different lipid content and
(Attrition: 6%)	CHO (Ref, n=15); • Full-fat dairy (FFD): ~36%	• LFD: 2.41± 0.31	<ul> <li>No adjustment for multiple comparisons</li> </ul>	fatty acid profiles in human
All baseline characteristics:	FAT, ~17% PRO, ~48%	40//400 11:10 5 005	No information on	milk.
(N=15, Mean± SEM)	CHO (n=15)	4:0 (g/100 g lipid), P<0.05	randomization, blinding, or	
Maternal age: 27± 1y	Maternal intake of 4 full-fat	<ul><li>(questioning this p-value)</li><li>FFD: 0.05± 0.00</li></ul>	carry-over effects	
Anthropometry:	or low-fat dairy products/d	• LFD: 0.05± 0.00	<ul> <li>Power calculation NR</li> </ul>	
Prepregnancy BMI: 24± 1	for 14d with 14d washout at	● LFD: 0.03± 0.00		
<ul> <li>Parity: 1.7± 0.2</li> </ul>	≥4mo postpartum	12:0 (~(100 ~ linid) D :0 05		
	<b>5</b>	12:0 (g/100 g lipid), P<0.05 • FFD: 4.58± 0.36		
	Dietary assessment	• LFD: 5.26± 0.44		
	methods: Dairy products delivered	♥ LFD. 3.20± 0.44		
	weekly to participants'	12:0 (a/100 a linid) D :0 004		
	homes with reminders of	13:0 (g/100 g lipid), P<0.001 • FFD: 0.04± 0.00		
	study guidelines and	• FFD: 0.04± 0.00 • LFD: 0.02± 0.00		
	sampling dates. 3d weighed	♥ LFD. 0.02± 0.00		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
	food records collected for 2	14:1 c9 (g/100 g lipid),		
	weekdays and 1 weekend	P<0.001		
	day at baseline and first	• FFD: 0.26± 0.01		
	week of each intervention period. Food records	• LFD: 0.15± 0.02		
	analyzed using the ESHA program.	Iso-14:0 (g/100 g lipid), P<0.001		
		• FFD: 0.03± 0.00		
	Outcomes: Human milk composition: Total lipids, fatty acids	• LFD: 0.01± 0.00		
	3 times every 14d at ≥4mo	15:0 (g/100 g lipid), P<0.001		
	postpartum	• FFD: 0.40± 0.01		
	postpartam	• LFD: 0.23± 0.02		
	Outcome assessment			
	methods:	Iso-15:0 (g/100 g lipid),		
	Milk was expressed	P<0.001		
	completely from one breast	• FFD: 0.07± 0.00		
	between 6:00-10:00h. Participants were instructed	• LFD: 0.03± 0.00		
	to refrain from human milk	Anteiso-15:0 (g/100 g lipid),		
	feeding and pumping for at least 3h prior to milk sample	P<0.001		
	donation.	• FFD: 0.12± 0.01		
		• LFD: 0.05± 0.01		
	Fatty acid extracted from			
	milk and lipid composition	16:0 (g/100 g lipid), P<0.001		
	by weight determined by gas chromatography.	• FFD: 21.62± 0.52		
	gas ciliomatography.	• LFD: 19.29± 0.58		
		lso-16:0 (g/100 g lipid),		
		P<0.001		
		• FFD: 0.09± 0.00		
		• LFD: 0.05± 0.01		
		16:1 t9 (g/100 g lipid),		
		16:1 t9 (g/100 g lipid), P<0.001		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		• FFD: 0.14± 0.01		
		• LFD: 0.08± 0.01		
		16:2 c9,c12 (g/100 g lipid),		
		P<0.05		
		• FFD: 0.22± 0.01		
		• LFD: 0.18± 0.01		
		17:0 (g/100 g lipid), P<0.001		
		• FFD: 0.37± 0.01		
		• LFD: 0.27± 0.01		
		Iso-17:0 (g/100 g lipid),		
		P<0.05		
		<ul> <li>FFD: 0.36± 0.01</li> </ul>		
		• LFD: 0.41± 0.01		
		Anteiso-17:0 (g/100 g lipid),		
		P<0.001		
		• FFD: 0.21± 0.01		
		• LFD: 0.11± 0.01		
		18:0 (g/100 g lipid), P<0.001		
		• FFD: 7.54± 0.27		
		• LFD: 5.75± 0.27		
		Anteiso-18:0 (g/100 g lipid),		
		P<0.001		
		• FFD: 0.05± 0.00		
		• LFD: 0.03± 0.00		
		Iso-18:0 (g/100 g lipid),		
		P<0.001		
		• FFD: 0.05± 0.01		
		• LFD: 0.03± 0.00		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		18:1 c11 (g/100 g lipid),		
		P<0.05		
		• FFD: 1.17± 0.15		
		• LFD: 1.32± 0.18		
		18:1 t11 (g/100 g lipid),		
		P<0.001		
		<ul> <li>FFD: 0.54± 0.03</li> </ul>		
		• LFD: 0.34± 0.03		
		18:2 c9,c12 (g/100 g lipid),		
		P<0.001		
		• FFD: 14.27± 0.75		
		• LFD: 18.80± 0.91		
		18:2 c9,t11(CLA) (g/100 g		
		lipid), P<0.001		
		• FFD: 0.33± 0.01		
		• LFD: 0.24± 0.01		
		18:3 α c9,c12,c15 (g/100 g		
		lipid), P<0.05		
		• FFD: 1.60± 0.12		
		• LFD: 1.97± 0.16		
		20:0 (g/100 g lipid), P<0.001		
		• FFD: 0.21± 0.02		
		• LFD: 0.16± 0.01		
		Non-significant:		
		Mean± SEM, Paired t-tests:		
		6:0 (g/100 g lipid), P=NS		
		• FFD: 0.08± 0.00		
		• LFD: 0.08± 0.01		
		8:0 (g/100 g lipid), P=NS		
		• FFD: 0.17± 0.01		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		• LFD: 0.17± 0.01		
		10:0 (g/100 g lipid), P=NS		
		• FFD: 1.11± 0.06		
		• LFD: 1.14± 0.06		
		14.0 (g/100 g lipid), P=NS		
		<ul> <li>FFD: 6.37± 0.38</li> </ul>		
		• LFD: 5.94± 0.54		
		16:1 c9 (g/100 g lipid),		
		P=NS		
		• FFD: 2.08± 0.15		
		• LFD: 2.21± 0.16		
		17:1 c9 (g/100 g lipid),		
		P=NS		
		• FFD: 0.04± 0.00		
		• LFD: 0.04± 0.00		
		18:1 c9 (g/100 g lipid),		
		P=NS		
		<ul> <li>FFD: 30.77± 0.80</li> </ul>		
		• LFD: 30.51± 0.59		
		18:1 c12 (g/100 g lipid),		
		P=NS		
		• FFD: 0.66± 0.14		
		• LFD: 0.69± 0.17		
		18:1 t7-8 (g/100 g lipid),		
		P=NS		
		• FFD: 0.31± 0.03		
		• LFD: 0.29± 0.05		
		18:1 t9 (g/100 g lipid), P=NS		

Study and Participant Characteristics	Intervention/Exposure and Outcomes	Results	Confounding and Study Limitations	Summary of findings
		• FFD: 0.32± 0.02		
		• LFD: 0.31± 0.03		
		18:1 t10 (g/100 g lipid),		
		P=NS		
		<ul> <li>FFD: 0.52± 0.05</li> </ul>		
		• LFD: 0.42± 0.05		
		18:3 γ c6,c9,c12 (g/100 g		
		lipid), P=NS		
		• FFD: 0.11± 0.01		
		• LFD: 0.13± 0.02		
		21:0 (g/100 g lipid), P=NS		
		• FFD: 0.05± 0.00		
		• LFD: 0.05± 0.01		
		22:0 (g/100 g lipid), P=NS		
		• FFD: 0.07± 0.01		
		<ul> <li>LFD: 0.06± 0.01</li> </ul>		

Table 3. Results from studies that assessed the relationship between dietary patterns during lactation and human milk fatty acid composition<sup>viii</sup>

Articles <sup>ix</sup>	Total milk fat	Saturated Fat	Monounsaturated fatty acids	Polyunsaturated fatty acids
<ul> <li>Tian, 2019<sup>7</sup></li> <li>Pattern 1: Mushroom food and algae, Meat, Marine products</li> </ul>	NR	SAT: Pattern 1: 40.38, Pattern 2: 42.92, Pattern 3: 39.10, Pattern 4: 42.92 (p<0.001)	MUFAs: Pattern 1: 34.40, Pattern 2: 33.53, Pattern 3: 34.85, Pattern 4: 33.45 (p=0.053)	PUFAs: Pattern 1: 24.49, Pattern 2: 22.09, Pattern 3: 24.63, Pattern 4: 22.77 (p=0.025)
<ul> <li>Pattern 2: Soybean products, Nuts, Dairy</li> <li>Pattern 3: Fruit, Vegetables</li> <li>Pattern 4: Grain/potato and beans, Eggs</li> </ul>				n-6 PUFAs: Pattern 1: 20.71, Pattern 2: 18.24, Pattern 3: 20.11, Pattern 4: 18.49 (p=0.038)
				n-3 PUFAs: Pattern 1: 3.96, Pattern 2: 3.55, Pattern 3: 3.56, Pattern 4: 3.86 (p=0.29)
				n-6: n-3 PUFA ratio: Pattern 1: 4.83, Pattern 2: 4.76, Pattern 3: 5.34, Pattern 4: 4.69 (p=0.34)
Perrin, 2019 <sup>6</sup>	Total Fat NS	SAT: Vegan: 33.1,	Data not reported as total	Data not reported as total
Vegan: Never/rarely consumed	Trans fat high ar among	Vegetarian: 40.0, Non- vegetarian: 42.3	MUFAs	PUFAs
<ul> <li>animal products</li> <li>Vegetarian: Never consumed meat; regularly consumed other animal products</li> <li>Non-vegetarian: Consumed meat sometimes/often</li> </ul>	Trans fat higher among women with Non-vegetarian > Vegetarian > Vegan diets (p<0.001)	(p<0.001)  C15:0, C16:0, C17:0, and C18:0 higher among	C14:1 cis, C16:1 cis, C17:1 cis higher among women with Non-vegetarian > Vegetarian	n-6 PUFAs: Vegan: 19.65, Vegetarian: 18.69, Non- vegetarian: 17.11 (NS)
		women with Non- vegetarian > Vegetarian > Vegan diets (p<0.001)	ian > Vegetarian n-3 n diets (p<0.001) Veg	n-3 PUFAs: Vegan: 2.29, Vegetarian: 1.55, Non- vegetarian: 1.46 (p<0.001)

viii AA: arachidonic acid, ALA: alpha-linolenic acid, DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid, LA: linoleic acid, MUFA: monounsaturated fatty acid, n-#: omega-#, NR: not reported, NS: non-significant, PUFA: polyunsaturated fatty acid, SAT: saturated fat

ix Data are Median % fatty acid proportions unless otherwise specified

Articles <sup>ix</sup>	Total milk fat	Saturated Fat	Monounsaturated fatty acids	Polyunsaturated fatty acids
	-	C8:0, C10:0, C12:0, C14:0, C20:0, C22:0, and C24:0 NS	Vegetarian > Non- vegetarian diets (p<0.001)	n-6: n-3 PUFA ratio: Vegan: 8.8, Vegetarian: 11.4, Non- vegetarian: 11.2 (p<0.001)
			C15:1 cis, C20:1 cis, C22:1 cis, C24:1 cis, C14:1 trans, C16:1 trans NS	LA:ALA ratio higher in Non- vegetarian > Vegetarian > Vegan diet C18:3 cis γ higher in Non- vegetarian > Vegetarian = Vegan
				ALA, and unsaturated fat higher among women with Vegan > Vegetarian > Non-vegetarian diets
				LA (C18:2 cis), C18:2 trans C20:2 cis, C20:3 cis, AA (C20:4), EPA (C20:5 cis), and DHA (C22:6 cis) NS

Table 4. Results from studies that assessed the relationship between diets based on macronutrient distributions during lactation and human milk composition<sup>x</sup>

Articles	Total milk fat	Saturated fat	Monounsaturated fatty acids	Polyunsaturated fatty acids
Mohammad, 2009 <sup>1</sup> High CHO (60% CHO, 25% FAT, 15% PRO) vs. High Fat (30% CHO, 55% FAT, 15% PRO)	Milk fat concentration and milk fat content/day higher after high fat diet (p<0.05)	NR	NR	NR
Mohammad, 2014 <sup>2xi</sup> High CHO (60% CHO, 25% FAT, 15% PRO) vs. High Fat (30% CHO, 55% FAT, 15% PRO)	Total milk fat higher in high fat diet (p<0.05) only in a fed state	∑SAT: Fasting: H-CHO: 15.71, H-FAT: 15.03 (NS) Feeding: H-CHO: 18.21, H- FAT: 18.37 (NS) Women during H-CHO diet had higher %total SAT (fed	∑MUFA: Fasting: H-CHO: 14.75, H-FAT: 15.78 (NS) Feeding: H-CHO: 13.37, H-FAT: 16.01 (p<0.01) Women during H-FAT diet had higher %Total MUFAs (both fed and fasting	ΣPUFA: Fasting: H-CHO: 11.45, H-FAT: 10.02 (NS) Feeding: H-CHO: 10.66, H-FAT: 12.52 (p<0.05) %Total PUFAs: NS Women during H-FAT diet had
		only p<0.05) and ∑C2:C14 (both fed and fasting	p<0.05)  Women during H-FAT diet had higher C18:1 than H-	higher C18:2 and C18:3 (fed only, p<0.01) and C20:2, C20:3, C20:4, C20:5, and C22:6 (fasting only, p<0.05)
		Women during H-CHO diet had higher C4:0, C6:0, C8:0, C10:0, C12:0 (fed only), C14:0, ∑C2:C14, C16:0 (fed only), C18:0 (fed only) in human milk (p<0.05) than H-FAT. C2:0 NS	CHO (fed only, p<0.01). C16:1 and C20:1 NS	than H-CHO. C22:5 NS

x AA: arachidonic acid, ALA: alpha-linolenic acid, CHO: carbohydrate, DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid, LA: linoleic acid, MUFA: monounsaturated fatty acid, n-#: omega-#, NR: not reported, NS: non-significant, PRO: protein, PUFA: polyunsaturated fatty acid, SAT: saturated fat, xi Units g/L

Articles	Total milk fat	Saturated fat	Monounsaturated fatty acids	Polyunsaturated fatty acids
Nasser, 2010 <sup>3xii</sup> High Fat (45.3% CHO, 40.3% FAT, 14.4%	NR	∑SAT: Low Fat: 41.1±0.82, High Fat: 40.4±0.85 (p=0.46)	ΣMUFA: Low Fat: 38.7±0.8, High Fat: 39.9±0.65 (p=0.10)	ΣPUFA: Low Fat: 16.9±0.66, High Fat: 16.4±0.48 (p=0.54)
PRO) vs Low Fat (68% CHO, 17.6% FAT, 14.4% PRO)	had higher total m chain FA, C10:0 a (p=0.01) in human than high fat. C18 C20:0 higher in hig than low fat diet (p	Women during low fat diet had higher total medium chain FA, C10:0 and C12:0 (p=0.01) in human milk than high fat. C18:0 and C20:0 higher in high fat diet	C16:1: Milk from women during low fat diet higher than high fat (p=0.046) C20:1: Milk from women during high fat diet higher than low fat (p=0.01)	Women during low fat diet had higher C18:3n-6, C20:3 and AA (C20:4n-6) in human milk than high fat milk (p<0.05). ALA (C18:3n:3) was higher in milk of mothers with high fat diet (p=0.01)
		than low fat diet (p=0.01). C14:0 and C16:0 NS	C14:1 and C18:1 NS	LA (C18:2n-6), C20:2n-6, C22:5n-3, EPA (C20:5n-3), DHA (C22:6n-3) NS
<b>Yahvah, 2015<sup>4xiii</sup></b> Low fat dairy	Total lipids was higher after a full-fat dairy diet	Data not reported as total saturated fat	Data not reported as total MUFAs	Data not reported as total PUFAs
(57% CHO, 24% FAT, 20% PRO) vs Full-fat dairy (48% CHO, 36% FAT, 17% PRO)	compared to low-fat dairy diet	Women during <u>full-fat dairy</u> diet had higher C13:0, iso-14:0, C15:0, iso-15:0, anteiso-15:0, C16:0, iso-C16:0, C17:0, anteiso 17:0, C18:0, anteiso 18:0, iso-18:0, C20:0 (p<0.05)	Women during full-fat dairy diet had higher C14:1, C16:1t9, C18:1t11 (p<0.001) Women during low-fat dairy diet had higher C18:1c11 (p<0.05) C16:1, C17:1, C18:1, C18:1, C18:1, C18:1t7-8, C18:1t9, C18:1t10 NS	Women during full-fat dairy diet had higher C16:2 and C18:2 c9,t11 (p<0.05) in human milk than low-fat dairy diet Women during low-fat dairy diet had higher C18:2 c9,c12 and
		Women during low fat dairy diet had higher C12:0 and iso-17:0 in their milk (p<0.05) C4:0, C6:0, C8:0, C10:0, C14:0, C21:0, C22:0 NS		C18:3α c9,c12,c15 than full-fat dairy diet (p<0.05) C18:3 γ c6,c9,c12 NS

xii Units g/100 g total fatty acids xiii Units g/100 g lipids

Table 5. Risk of bias for randomized controlled trials examining dietary patterns during lactation and human milk composition and quantity<sup>xiv, xv</sup>

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Mohammad, 2014 <sup>2</sup>	Some concerns	Some concerns	Low	Low	Some concerns
Mohammad, 2009 <sup>1</sup>	Some concerns	Some concerns	Low	Low	Some concerns
Nasser, 2010 <sup>3</sup>	Low	Some concerns	Low	Low	Some concerns
Yahvah, 2015⁴	Some concerns	Some concerns	Low	Low	Some concerns

Table 6. Risk of bias for observational studies examining dietary patterns during lactation and human milk composition and quantity<sup>xvi</sup>

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Tian, 2019 <sup>7</sup>	Serious	Serious	Moderate	Low	Low	Low	Moderate
Pawlak, 2018 <sup>5</sup>	Critical	Serious	Serious	Critical	Low	Low	Moderate
Perrin, 2019 <sup>6</sup>	Critical	Serious	Serious	Critical	Low	Low	Moderate

xiv A detailed description of the methodology used for assessing risk of bias is available on the NESR website: <a href="https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews">https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews</a> and in Part C of the following reference: Dietary Guidelines Advisory Committee: 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

xv Possible ratings of low, some concerns, or high determined using the "Cochrane Risk-of-bias 2.0" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. *Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.)

<sup>&</sup>lt;sup>xvi</sup> Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

## **METHODOLOGY**

The NESR team used its rigorous, protocol-driven methodology to support the 2020 Dietary Guidelines Advisory Committee in conducting this systematic review.

NESR's systematic review methodology involves:

- Developing a protocol,
- Searching for and selecting studies,
- Extracting data from and assessing the risk of bias of each included study,
- Synthesizing the evidence,
- Developing conclusion statements,
- Grading the evidence underlying the conclusion statements, and
- Recommending future research.

A detailed description of the methodology used in conducting this systematic review is available on the NESR website: <a href="https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews">https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews</a>, and can be found in the 2020 Dietary Guidelines Advisory Committee Report, Part C: Methodology. This systematic review was peer reviewed by Federal scientists, and information about the peer review process can also be found in the Committee's Report, Part C. Methodology. Additional information about this systematic review, including a description of and rationale for any modifications made to the protocol can be found in the 2020 Dietary Guidelines Advisory Committee Report, Chapter 3. Food, Beverage, and Nutrient Consumption During Lactation.

Below are details of the final protocol for the systematic review described herein, including the:

- Analytic framework
- Literature search and screening plan
- Literature search and screening results

### ANALYTIC FRAMEWORK

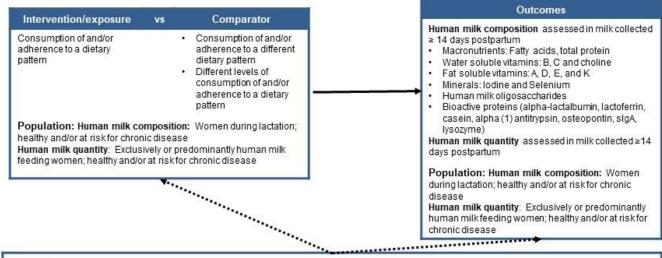
The analytic framework (**Figure 1**) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The inclusion and exclusion criteria that follow provide additional information about how parts of the analytic framework were defined and operationalized for the review.

<sup>-</sup>

xvii Dietary Guidelines Advisory Committee. 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

Figure 1. Analytic framework

Systematic review question: What is the relationship between dietary patterns consumed during lactation and human milk composition and quantity?



Key Confounders: Age, Race/ethnicity, Socioeconomic status, Anthropometry (obesity status during lactation and gestational weight gain), Smoking, Parity, Gestational age, Supplement intake during lactation

#### Key definitions

Dietary Pattern – The quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.

Exclusive human milk feeding - Infant receives no other food or drink, not even water, except breast milk (including milk expressed or from a wet nurse). Infants may receive oral rehydration solution, drops and syrups (vitamins, minerals and medicines). (WHO, 2001)

Predominant human milk feeding — Breast milk (including milk expressed or from a wet nurse) is infant's predominant source of nourishment. Infants may also receive liquids (water and water-based drinks, fruit juices) ritual fluids and oral rehydration solution, drops or syrups (vitamins, minerals and medicines). (WHO, 2001)

#### Legend

■ The relationship of interest in the systematic review

Factors that may impact the relationship of interest in the systematic review

# LITERATURE SEARCH AND SCREENING PLAN

# Inclusion and exclusion criteria

This table provides the inclusion and exclusion criteria for the systematic review. The inclusion and exclusion criteria are a set of characteristics used to determine which articles identified in the literature search were included in or excluded from the systematic review.

Table 7. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria		
Study design	<ul> <li>Randomized controlled trials</li> <li>Non-randomized controlled trials including quasi-experimental and controlled before-and-after studies</li> <li>Prospective cohort studies</li> <li>Retrospective cohort studies</li> <li>Nested case-control studies</li> <li>Cross-sectional studies</li> </ul>	<ul> <li>Uncontrolled trials</li> <li>Case-control studies</li> <li>Narrative reviews</li> <li>Systematic reviews</li> <li>Meta-analyses</li> </ul>		
Intervention/ exposure	of and/or adherence to a  1. Dietary pattern [i.e., the quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed] including, at a minimum, a description of the foods and beverages in the pattern	Studies that     1a. Do not provide a description of the dietary pattern, which at minimum, must include the foods and beverages in the pattern (i.e., studies that examine a labeled dietary pattern, but do not describe the foods and beverages consumed)		
	<ul> <li>2. Diet based on macronutrient distribution outside of the AMDR and</li> <li>Include the macronutrient distribution of carbohydrate, fat, and protein of the diet, and</li> <li>Include at least one macronutrient outside of the acceptable macronutrient</li> </ul>	macronutrient distribution of the diet (i.e., studies that only examine a single macronutrient in relation to		

Category	Inclusion Criteria	Exclusion Criteria
	distribution range (AMDR <sup>xviii</sup> )	
Comparator	<ul> <li>Dietary patterns described by foods and beverages consumed:</li> <li>Consumption of and/or adherence to a different dietary pattern</li> <li>Different levels of consumption of and/or adherence to a dietary pattern</li> <li>Diets described by macronutrient distribution:</li> <li>Different macronutrient distribution</li> </ul>	<ul> <li>No comparator</li> <li>Macronutrient proportion(s) of interest also outside the AMDR</li> </ul>
Outcomes	<ul> <li>Human milk composition assessed in milk collected ≥ 14 days postpartum</li> <li>Macronutrients: Fatty acids, total protein</li> <li>Water soluble vitamins: B, C, and choline</li> <li>Fat soluble vitamins: A, D, E, K</li> <li>Minerals: Iodine and Selenium</li> <li>Human milk oligosaccharides</li> <li>Bioactive components</li> <li>Human milk quantity assessed in milk collected ≥14 days postpartum</li> </ul>	

xviii Macronutrient percent of energy outside of the AMDR are as follows:

<sup>•</sup> Carbohydrate for all age groups: < 45 or > 65 percentage of energy;

Protein (age 19 years and older): < 10 or > 35 percentage of energy;

<sup>•</sup> Fat (age 19 years and older): < 20 or > 35 percentage of energy.

Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Washington, DC: The National Academies Press; 2002.

Category	Inclusion Criteria	Exclusion Criteria
Date of publication	January 2000 to November 2019	<ul> <li>Articles published before January 2000 or after November 2019</li> </ul>
Publication status	Articles published in peer-reviewed journals	<ul> <li>Articles that have not been peer- reviewed and are not published in peer-reviewed journals, including unpublished data, manuscripts, reports, abstracts, and conference proceedings</li> </ul>
Language of publication	Articles published in English	<ul> <li>Articles published in languages other than English</li> </ul>
Countryxix	<ul> <li>Studies conducted in Very High or High Human Development Countries</li> </ul>	<ul> <li>Studies conducted in countries ranked as medium or lower human development</li> </ul>
Study participants	<ul> <li>Human milk composition: Women during lactation</li> <li>Human milk quantity: Exclusively or predominantly human milk feeding women</li> </ul>	<ul> <li>Animal and in vitro models</li> <li>Studies that ONLY enroll multiple gestation pregnancies or present ONLY combined analyses of singleton and multiple gestations (human milk quantity outcome only)</li> </ul>
Health status of study participants	<ul> <li>Studies that enroll mothers who are healthy and/or at risk for chronic disease</li> <li>Studies that enroll some mothers diagnosed with a disease</li> <li>Studies that enroll some mothers who were severely undernourished prior to pregnancy</li> <li>Studies that enroll some or all mothers classified as underweight, or obese prior to pregnancy</li> </ul>	<ul> <li>Studies that ONLY enroll mothers who gave birth to preterm (gestational age &lt;37 weeks and 0/7 days)</li> <li>Studies that ONLY enroll mothers diagnosed with a disease, including severe undernutrition, or hospitalized with an illness or injury</li> </ul>

xix The Human Development classification was based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data were collected (UN Development Program, HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: http://hdr.undp.org/en/data). If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank was used instead (The World Bank. World Bank country and lending groups. Available from:

https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-country-and-lending-groups).

### **Electronic databases and search terms**

#### **PubMed**

- Provider: U.S. National Library of Medicine
- Date(s) Searched: November 13, 2019
- Date range searched: January 1, 2000 November 13, 2019
- Search Terms:

#1 - "Lactation" [Mesh] OR lactation[tiab] OR lactating[tiab] OR "Breast Feeding" [Mesh] OR breastfeeding[tiab] OR breast-feeding[tiab] OR breast-feed\* [tiab] OR breast-feed\* [tiab] OR breast-feed[tiab] OR breast-feed[tiab] OR breast-feed\* OR nursing women[tiab]

#2 - dietary pattern\* OR diet pattern\* OR eating pattern\* OR food pattern\* OR diet quality[tiab] OR eating habit\*[tiab] OR dietary habit\* OR diet habit\* OR food habit\* OR "Feeding Behavior" [Mesh] OR feeding behavior\*[tiab] OR beverage consumption[tiab] OR beverage habit\*[tiab] OR beverage intake\*[tiab] OR dietary profile\* OR food profile[tiab] OR diet profile\* OR eating profile\* OR dietary guideline\* OR dietary recommendation\* OR dietary intake[tiab] OR food intake[tiab] OR food consumption[tiab] OR dietary consumption[tiab] OR eating frequenc\* OR food frequenc\*[tiab] OR eating style\*[tiab] OR dietary change\*[tiab] OR dietary choice\*[tiab] OR food choice\*[tiab] OR "Diet, Mediterranean"[Mesh] OR Mediterranean Diet\*[tiab] OR "Dietary Approaches To Stop Hypertension"[Mesh] OR Dietary Approaches To Stop Hypertension Diet\* OR DASH diet\* OR "Diet, Gluten-Free" [Mesh] OR Gluten Free diet\* OR prudent diet\* OR "Diet, Paleolithic" [Mesh] OR Paleolithic Diet\* OR "Diet, Vegetarian" [Mesh] OR vegetarian diet\*[tiab] OR vegan diet\* OR "Diet, Healthy" [Mesh] OR plant based diet\* OR "Diet, Western" [Mesh] OR western diet\* OR "Diet, Carbohydrate-Restricted"[Mesh] OR low-carbohydrate diet\* OR high carbohydrate diet\* OR Ketogenic Diet\* OR Nordic Diet\* OR "Diet, Fat-Restricted" [Mesh] OR "Diet, High-Fat" [Mesh] OR "Diet, High-Protein"[Mesh] OR high protein diet\*[tiab] OR high-fat diet\* [tiab] OR low fat diet\*[tiab] OR "Diet, Protein-Restricted" [Mesh] OR low protein diet\* OR "Diet, Sodium-Restricted" [Mesh] OR low-sodium diet\* OR low salt diet\* OR (("Dietary Proteins"[Mesh] OR dietary protein\*[tiab] OR "Dietary Carbohydrates" [Mesh] OR dietary carbohydrate\*[tiab] OR "Dietary Fats" [Mesh] OR dietary fat\*[tiab] OR hypocaloric OR hypo-caloric) AND (diet[tiab] OR diets[tiab] OR consumption[tiab] OR intake[tiab] OR supplement\*[tiab])) OR ("Guideline Adherence"[Mesh] AND (diet[tiab] OR dietary[tiab] OR food[tiab] OR beverage[tiab])) OR (diet score\* OR diet quality score\* OR diet quality index\* OR dietary habits score\* OR kidmed OR diet index\* OR dietary index\* OR Food-based Index\* OR diet quality index\* OR food index\* OR food score\* OR Mediterranean diet score\* OR MedDietScore OR healthy eating index[tiab] OR food frequency questionnaire\* OR food frequency survey\* OR "Nutrition Surveys" [Mesh] OR nutrition survey\*[tiab] OR diet survey\*[tiab] OR food survey\* OR dietary questionnaire[tiab]) OR ((pattern[tiab] OR patterns[tiab] OR consumption[tiab] OR habit\*[tiab]) AND ("Diet"[Mesh:NoExp] OR diet[tiab] OR diets[tiab] OR dietary[tiab] OR "Food"[Mesh] OR food[tiab] OR foods[tiab] OR "Beverages"[Mesh] OR beverage[tiab] OR beverages[tiab]))

#3 - "human milk composition" [tiab] OR "Milk, Human" [Mesh] OR "milk composition" [tiab] OR "Nutrients" [Mesh: NoExp] OR macronutrient\* [tiab] OR "Vitamins" [Mesh] OR "Vitamins" [Pharmacological Action] OR vitamin\* [tiab] OR "Milk Proteins" [Mesh] OR total protein\* [tiab] OR "milk protein\*" [tiab] OR lactoferrin\* [tiab] OR lactal bumin [tiab] OR casein\* [tiab] OR whey protein\* [tiab] OR "alpha 1-Antitrypsin" [Mesh] OR alpha 1-antitrypsin\* [tiab] OR "alpha 1-Antitrypsin Deficiency" [Mesh] OR "alpha 1-Antitrypsin Deficien\* [tiab] OR

"Osteopontin"[Mesh] OR osteopontin\*[tiab] OR "IgA Deficiency"[Mesh] OR "Immunoglobulin A"[Mesh] OR iga[tiab] OR "iga 1"[tiab] OR "iga 2"[tiab] OR lysozyme\*[tiab] OR "Muramidase"[Mesh]

#4 - fatty acid\*[tiab] OR "Fatty Acids"[Mesh:noexp] OR "Fatty Acids, Unsaturated"[Mesh:noexp] OR Arachidonic acid\*[tiab] OR linolenic acid\*[tiab] OR linolenic acid\*[tiab] OR Docosahexaenoic Acid\*[tiab] OR Eicosapentaenoic Acid\*[tiab] OR gamma-Linolenic Acid\*[tiab] OR "Arachidonic Acids"[Mesh] OR "Fatty Acids, Essential"[Mesh] OR "Fatty Acids, Omega-3"[Mesh] OR "Fatty Acids, Omega-6"[Mesh] OR pufa[tiab] OR pufas[tiab] OR alpha-Linolenic Acid[tiab] OR "Fatty Acids, Essential"[Mesh] OR "Linolenic Acids"[Mesh] OR "Trans Fatty Acids"[Mesh] OR "Fatty Acids, Monounsaturated"[Mesh]

#5 - "Vitamin B Complex" [Mesh] OR "Vitamin B Complex" [Pharmacological Action] OR "Vitamin B 12" [Mesh] OR "Vitamin B 12" [tiab] OR "Vitamin B 12" [tiab] OR "Vitamin B 12" [tiab] OR "Vitamin B 12" [Deficiency" [Mesh] OR "vitamin b" [tiab] OR "vitamin c" [tiab] OR "Ascorbic Acid" [Mesh] OR "ascorbic acid" [tiab] OR choline [tiab] OR "Choline [Mesh] OR "vitamin A" [tiab] OR "vitamin D" [tiab] OR "vitamin C" [tiab] OR "Vitamin A" [Mesh] OR retinol [tiab] OR "Vitamin A Deficiency [Mesh] OR "Ascorbic Acid Deficiency [Mesh] OR "Vitamin E" [Mesh] OR "Vitamin D" [Mesh] OR "Vitamin CD [Mesh] OR "Vitamin K" [Mesh] OR "Vitamin CD [Mesh]

#6 - #1 AND #2

#7 - #3 OR #4 OR #5

#8 - #6 AND #7

#9 - #8 NOT (("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti])

Filters: Publication date from 2000/01/01 to 2019/11/13; English

## **Cochrane Central Register of Controlled Trials (CENTRAL)**

- Provider: John Wiley & Sons
- Date(s) Searched: November 14, 2019
- Date range searched: January 1, 2000 November 14, 2019
- Search Terms:

#1 - [mh Lactation] OR lactation OR lactating OR [mh "breast feeding"] OR breastfeeding OR "breast feed" OR "breast feeds" OR breast-feed OR

- #2 ("dietary pattern\*" OR "diet pattern\*" OR "eating pattern\*" OR "food pattern\*" OR "diet quality" OR "eating habit\*" OR "dietary habit\*" OR "diet habit\*" OR "food habit\*" OR [mh "Feeding Behavior"] OR "feeding behavior\*" OR "beverage consumption" OR "beverage habit\*" OR "beverage intake\*" OR "dietary profile\*" OR "food profile" OR "diet profile\*" OR "eating profile\*" OR "dietary guideline\*" OR "dietary recommendation\*" OR "dietary intake" OR "food intake" OR "food consumption"):ti,ab OR "dietary consumption" OR "eating frequenc\*" OR "food frequenc\*" OR "eating style\*" OR "dietary change\*" OR "dietary choice\*" OR "food choice\*" OR [mh "Diet, Mediterranean"] OR "Mediterranean Diet\*" OR [mh "Dietary Approaches To Stop Hypertension"] OR "Dietary Approaches To Stop Hypertension Diet\*" OR "DASH diet\*" OR [mh "Diet, Gluten-Free"] OR "Gluten Free diet\*" OR "prudent diet\*" OR [mh "Diet, Paleolithic"] OR "Paleolithic Diet\*" OR [mh "Diet, Vegetarian"] OR "vegetarian diet\*" OR "vegan diet\*" OR [mh "Diet, Healthy"] OR "plant based diet\*" OR [mh "Diet, Western"] OR "western diet\*" OR [mh "Diet, Carbohydrate-Restricted"] OR "low carbohydrate diet\*" OR "high carbohydrate diet\*" OR "Ketogenic Diet\*" OR "Nordic Diet\*" OR [mh "Diet, Fat-Restricted"] OR [mh "Diet, High-Fat"] OR [mh "Diet, High-Protein"] OR "high protein diet\*" OR "high fat diet\*" OR "low fat diet\*" OR [mh "Diet, Protein-Restricted"] OR "low protein diet\*" OR [mh "Diet, Sodium-Restricted"] OR "low sodium diet\*" OR "low salt diet\*" OR (([mh "Dietary Proteins"] OR "dietary protein\*" OR [mh "Dietary Carbohydrates"] OR "dietary carbohydrate\*" OR [mh "Dietary Fats"] OR "dietary fat\*" OR hypocaloric OR hypo-caloric) NEAR (diet OR diets OR consumption OR intake OR supplement\*)) OR ("guideline adherence") NEAR (diet OR dietary OR food OR beverage)) OR ("diet score" OR "diet scores" OR "diet quality score" OR "diet quality scores" OR "diet quality index" OR "dietary habits score" OR kidmed OR "diet index" OR "dietary index" OR "Food-based Index" OR "diet quality index" OR "food index" OR "food score" OR "food scores" OR "Mediterranean diet score" OR MedDietScore OR "healthy eating index" OR "food frequency questionnaire" OR "food frequency questionnaires" OR "food frequency survey" OR "food frequency surveys" OR [mh "Nutrition Surveys"] OR "nutrition survey" OR "nutrition surveys" OR "diet survey" OR "diet surveys" OR "food survey" OR "food surveys" OR "dietary questionnaire"):ti,ab,kw OR ((pattern OR patterns OR consumption OR habit\*) NEAR ([mh ^Diet] OR diet OR diets OR dietary OR [mh Food] OR food OR foods OR [mh Beverages] OR beverage OR beverages))):ti,ab,kw
- #3 ([mh "milk, human"] OR "breast milk" OR "human milk" OR "mother's milk" OR breastmilk OR "human milk" OR "maternal milk" OR (milk NEAR/6 composition) OR [mh "nutrients"] OR macronutrient\* OR [mh "vitamins"] OR vitamin\* OR [mh "milk proteins"] OR "total protein" OR "total proteins" OR "milk protein\*" OR lactoferrin\* OR lactalbumin\* OR casein\* OR "whey protein\*" OR "alpha 1 antitrypsin\*" OR [mh osteopontin] OR osteopontin\* OR [mh "IgA Deficiency"] OR [mh "Immunoglobulin A"] OR iga1 OR iga2 OR iga OR lysozyme\* OR [mh muramidase]):ti,ab,kw
- #4 ("fatty acid\*" OR [mh ^"Fatty Acids"] OR [mh ^"Fatty Acids, Unsaturated"] OR "Arachidonic acid\*" OR "linolenic acid\*" OR "linoleic acid\*" OR "Docosahexaenoic Acid\*" OR "Eicosapentaenoic Acid\*" OR gamma-linolenic acid\* OR [mh "Arachidonic Acids"] OR [mh "Fatty Acids, Essential"] OR [mh "Fatty Acids, Omega-3"] OR [mh "Fatty Acids, Omega-6"] OR "omega-6 fatty acid\*" OR "omega-3 fatty acid\*" OR "omega 6 fatty acid\*" OR "omega 3 fatty acid\*" OR pufa OR pufas OR "alpha-linolenic acid\*" OR [mh "Fatty Acids, Essential"] OR [mh "Linolenic Acids"] OR [mh "Trans Fatty Acids"] OR [mh "Fatty Acids,

## Monounsaturated"]):ti,ab

#5 - ([mh "vitamin b complex"] OR [mh "Vitamin B 12"] OR "Vitamin B 12" OR "Vitamin B 12" OR [mh "Vitamin B 12 Deficiency"] OR "vitamin b" OR "vitamin c" OR [mh "ascorbic acid"] OR "ascorbic acid\*" OR choline OR [mh choline] OR "vitamin A" OR "vitamin E" OR "vitamin D" OR "vitamin K" OR [mh "vitamin A"] OR retinol OR [mh "vitamin A deficiency"] OR [mh "ascorbic acid deficiency"] OR [mh "vitamin E"] OR [mh "vitamin E deficiency"] OR tocopheral\* OR [mh "Vitamin D"] OR [mh "vitamin D deficiency"] OR [mh cholecalciferol] OR cholecalciferol\* OR [mh ergocalciferols] OR ergocalciferol\* OR [mh "vitamin K"] OR [mh vitamin K deficiency"] OR [mh iodine] OR iodine\* OR [mh selenium] OR selenium OR [mh oligosaccharides] OR oligosaccharide\* OR (milk NEAR/5 (amount OR quantity))):ti,ab

#6 - #1 AND #2

#7 - #3 OR #4 OR #5

#8 - #6 AND #7

Filters: Publication Year from 2000 – 2019, Trials

#### **Embase**

Provider: Elsevier

• Date(s) Searched: November 13, 2019

Date range searched: January 1, 2000 – November 13, 2019

Search Terms:

#1 - ('breast feeding'/exp OR 'lactation'/exp OR lactation:ti,ab OR lactating:ti,ab OR breastfeeding:ti,ab OR 'breast feed':ti,ab OR breastfeed:ti,ab OR 'breast feed':ti,ab OR breastfeed\*:ti,ab OR 'nursing women':ti,ab OR 'nursing mother\*':ti,ab)

#2 - 'feeding behavior'/exp OR 'mediterranean diet'/de OR 'dash diet'/de OR 'gluten free diet'/exp OR 'paleolithic diet'/de OR 'vegetarian diet'/exp OR 'healthy diet'/de OR 'western diet'/de OR 'low carbohydrate diet'/exp OR 'low fat diet'/de OR 'lipid diet'/exp OR 'protein diet'/exp OR 'protein restriction'/de OR 'sodium restriction'/de OR 'dietary pattern\*':ab,ti OR 'diet pattern\*':ab,ti OR 'eating pattern\*':ab,ti OR 'food pattern\*':ab,ti OR 'diet quality':ab,ti OR 'eating habit\*':ab,ti OR 'dietary habit\*':ab,ti OR 'diet habit\*':ab,ti OR 'food habit\*':ab,ti OR 'feeding behavior\*':ab,ti OR 'beverage consumption':ab,ti OR 'beverage habit\*':ab,ti OR 'beverage intake\*':ab,ti OR 'dietary profile\*':ab,ti OR 'food profile':ab,ti OR 'diet profile\*':ab,ti OR 'eating profile\*':ab,ti OR 'dietary guideline\*':ab,ti OR 'dietary recommendation\*':ab,ti OR 'dietary intake':ab,ti OR 'food intake':ab,ti OR 'food consumption':ab,ti OR 'dietary consumption':ab,ti OR 'eating frequenc\*':ab,ti OR 'food frequenc\*':ab,ti OR 'eating style\*':ab,ti OR 'dietary change\*':ab,ti OR 'dietary choice\*':ab,ti OR 'food choice\*':ab,ti OR 'mediterranean diet\*':ab,ti OR 'dietary approaches to stop hypertension diet\*':ab,ti OR 'dash diet\*':ab,ti OR 'gluten free diet\*':ab,ti OR 'prudent diet\*':ab,ti OR 'paleolithic diet\*':ab,ti OR 'vegetarian diet\*':ab,ti OR 'vegan diet\*':ab,ti OR 'plant based diet\*':ab,ti OR 'western diet\*':ab,ti OR 'lowcarbohydrate diet\*':ab.ti OR 'high carbohydrate diet\*':ab.ti OR 'ketogenic diet\*':ab.ti OR 'nordic diet\*':ab,ti OR 'high protein diet\*':ab,ti OR 'high-fat diet\*':ab,ti OR 'low fat diet\*':ab,ti OR 'low

protein diet\*':ab,ti OR 'low-sodium diet\*':ab,ti OR 'low salt diet\*':ab,ti OR ((('dietary protein\*' OR 'dietary carbohydrate\*' OR 'dietary fat\*' OR hypocaloric OR 'hypo caloric') NEAR/6 (diet OR diets OR consumption OR intake OR supplement\*)):ab,ti) OR (('guideline adherence' NEAR/6 (diet OR dietary OR food OR beverage)):ab,ti) OR 'diet score\*':ab,ti OR 'diet quality score\*':ab,ti OR 'dietary habits score\*':ab,ti OR kidmed:ab,ti OR 'diet index\*':ab,ti OR 'dietary index\*':ab,ti OR 'food-based index\*':ab,ti OR 'diet quality index\*':ab,ti OR 'food index\*':ab,ti OR 'food score\*':ab,ti OR 'mediterranean diet score\*':ab,ti OR meddietscore:ab,ti OR 'healthy eating index':ab,ti OR 'food frequency questionnaire\*':ab,ti OR 'food frequency survey\*':ab,ti OR 'nutrition survey\*':ab,ti OR 'diet survey\*':ab,ti OR 'food survey\*':ab,ti OR 'dietary questionnaire':ab,ti OR (((pattern OR patterns OR consumption OR habit\*) NEAR/6 (diet OR diets OR dietary OR food OR foods OR beverage OR beverages)):ab,ti)

- #3 ('breast milk'/exp OR 'breast milk':ti,ab OR 'human milk':ti,ab OR 'mothers milk':ti,ab OR breastmilk:ti,ab OR 'maternal milk':ti,ab) OR (milk NEAR/5 composition) OR 'nutrient'/exp OR macronutrient\*:ti,ab OR 'vitamin'/exp OR vitamin\*:ti,ab OR 'milk protein'/exp OR total) AND protein\*:ti,ab OR 'milk protein\*:ti,ab OR 'milk protein'/exp OR 'lactoferrin'/exp OR lactoferrin\*:ti,ab OR 'lactalbumin'/exp OR lactalbumin:ti,ab OR casein\*:ti,ab OR 'whey protein\*:ti,ab OR 'alpha 1 antitrypsin\*:ti,ab OR 'alpha 1 antitrypsin deficiency'/exp OR 'osteopontin'/exp OR osteopontin\*:ti,ab OR iga:ti,ab OR 'iga 1':ti,ab OR 'lactalbumin adeficiency'/exp OR 'immunoglobulin adeficiency'/exp OR 'immunoglobulin a'/exp OR 'immunoglobulin a':ti,ab OR 'lysozyme'/exp
- #4 'fatty acid\*':ti,ab OR 'fatty acid'/de OR 'unsaturated fatty acid'/de OR 'arachidonic acid'/exp OR 'arachidonic acid\*':ti,ab OR 'linolenic acid\*':ti,ab OR 'linolenic acid\*':ti,ab OR 'linolenic acid\*':ti,ab OR 'gamma linolenic acid\*':ti,ab OR 'omega 3 fatty acid'/exp OR 'omega 3 fatty acid\*':ti,ab OR 'omega-6 fatty acid'/exp OR 'omega 6 fatty acid\*':ti,ab OR pufa:ti,ab OR pufas:ti,ab OR 'alpha linolenic acid\*':ti,ab OR 'monounsaturated fatty acid'/exp OR 'essential fatty acid'/exp OR 'linolenic acid'/exp OR 'trans fatty acid'/exp OR 'trans fatty acid\*':ti,ab OR 'monounsaturated fatty acid\*':ti,ab OR 'monounsaturated fatty acid\*':ti,ab OR 'monounsaturated fatty acid\*':ti,ab OR 'monounsaturated fatty acid\*':ti,ab
- #5 'vitamin b 12':ti,ab OR 'vitamin b12':ti,ab OR 'vitamin b':ti,ab OR 'vitamin c':ti,ab OR 'ascorbic acid\*':ti,ab OR choline:ti,ab OR vitamin a':ti,ab OR vitamin e':ti,ab OR vitamin d':ti,ab OR vitamin k':ti,ab OR retinol:ti,ab OR tocopherol\*:ti,ab OR cholecalciferol\*:ti,ab OR ergocalciferol\*:ti,ab OR iodine\*:ti,ab OR selenium:ti,ab OR oligosaccharide\*:ti,ab OR (milk NEAR/5 (amount OR quantity OR quality)) OR 'vitamin b complex'/exp OR 'cyanocobalamin'/exp OR 'b12 deficiency'/exp OR 'ascorbic acid'/exp OR 'choline'/exp OR 'retinol'/exp OR 'retinol deficiency'/exp OR 'ascorbic acid deficiency'/exp OR 'alpha tocopherol'/exp OR 'alpha tocopherol deficiency'/exp OR 'vitamin d'/exp OR 'vitamin d'deficiency'/exp OR 'colecalciferol'/exp OR 'ergocalciferol'/exp OR vitamin k group'/exp OR 'iodine'/exp OR 'selenium'/exp OR 'oligosaccharide'/exp

#6 - #1 AND #2

#7 - #3 OR #4 OR #5

**#8 -** #6 AND #7

#9 - #8 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2000-2019]/py NOT ([conference abstract]/lim OR [conference paper]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

## **Cumulative Index of Nursing and Allied Health Literature (CINAHL Plus)**

Provider: EBSCOhost

• Date(s) Searched: November 14, 2019

Date range searched: January 1, 2000 – November 14, 2019

Search Terms:

**#1 -** MH "Breast Feeding" OR breastfeeding OR breast-feeding OR MH Lactation OR lactation OR lactation OR lactation OR breastfeeding OR "breast feed\*" OR breast-feed\* OR breastfeed OR breastfeed OR "nursing women" OR "nursing mother\*"

#2 - "dietary pattern\*" OR "diet pattern\*" OR "eating pattern\*" OR "food pattern\*" OR "diet quality" OR "eating habit\*" OR "dietary habit\*" OR "diet habit\*" OR "food habit\*" OR MH "Eating Behavior+" OR "feeding behavior\*" OR "beverage consumption" OR "beverage habit\*" OR "beverage intake\*" OR "dietary profile\*" OR "food profile\*" OR "diet profile\*" OR "eating profile\*" OR "dietary guideline\*" OR "dietary recommendation\*" OR "dietary intake\*" OR "food intake\*" OR "food consumption" OR "dietary consumption" OR "eating frequenc\*" OR "food frequenc\*" OR "eating style\*" OR "dietary change\*" OR "dietary choice\*" OR "food choice\*" OR MH "Diet, Mediterranean" OR "Mediterranean Diet\*" OR MH "Dietary Approaches To Stop Hypertension" OR "Dietary Approaches To Stop Hypertension Diet\*" OR "DASH diet\*" OR MH "Diet, Gluten-Free" OR "Gluten Free diet\*" OR "prudent diet\*" OR MH "Diet, Paleolithic" OR "Paleolithic Diet\*" OR MH "Diet, Vegetarian" OR "vegetarian diet\*" OR "vegan diet\*" OR MH "Healthy Diet" OR "plant based diet\*" OR MH "Diet, Western" OR "western diet\*" OR MH "Diet, Carbohydrate-Restricted" OR "low-carbohydrate diet\*" OR "high carbohydrate diet\*" OR "Ketogenic Diet\*" OR "Nordic Diet\*" OR MH "Diet, Fat-Restricted" OR MH "Diet, High-Fat" OR MH "Diet, High-Protein" OR "high protein diet\*" OR "high-fat diet\*" OR "low fat diet\*" OR MH "Diet, Protein-Restricted" OR "low protein diet\*" OR MH "Diet, Sodium-Restricted" OR "low-sodium diet\*" OR "low salt diet\*" OR ((MH "Dietary Proteins" OR "dietary protein\*" OR MH "Dietary Carbohydrates" OR "dietary carbohydrate\*" OR MH "Dietary Fats" OR "dietary fat\*" OR hypocaloric OR hypo-caloric) AND (diet OR diets OR consumption OR intake OR supplementation)) OR (MH "Guideline Adherence" AND (diet OR dietary OR food OR beverage)) OR ("diet score\*" OR "diet quality score\*" OR "diet quality index\*" OR "dietary habits score\*" OR kidmed OR "diet index\*" OR "dietary index\*" OR "Food-based Index\*" OR "diet quality index\*" OR "food index\*" OR "food score\*" OR "Mediterranean diet score\*" OR MedDietScore OR "healthy eating index" OR "food frequency questionnaire\*" OR "food frequency survey\*" OR MH "Nutrition Surveys" OR "nutrition survey\*" OR "diet survey\*" OR "food survey\*" OR "dietary questionnaire\*") OR ((pattern OR patterns OR consumption OR habit\*) AND (MH "Diet" OR diet OR diets OR dietary OR MH "Food" OR food OR foods OR MH "Beverages" OR beverage OR beverages))

#3 - MH "Milk, Human" OR "breast milk" OR breast-milk OR "human milk" OR "mother's milk" OR "mothers milk" OR "human milk composition" OR (milk n5 composition) OR (MH "Nutrients") OR "macronutrients" OR (MH "Vitamins") OR "vitamin\*" OR (MH "milk proteins") OR "total protein\*" OR "milk protein\*" OR lactoferrin\* OR lactalbumin\* OR casein\* OR "whey

protein\*" OR "alpha 1-antitrypsin\*" OR osteopontin\* OR iga OR "iga 1" OR "iga 2" OR "immunoglobulin a" OR lysozyme\* OR muramidase\*

#4 - (MH "Fatty Acids") OR "fatty acid\*" OR (MH "Fatty Acids, Omega-6+") OR (MH "Fatty Acids, Omega-3+") OR (MH "Fatty Acids, Unsaturated+") OR (MH "Fatty Acids, Monounsaturated+") OR (MH "Trans Fatty Acids+") OR (MH "Fatty Acids, Essential+") OR "fatty acids" OR "arachidonic acid\*" OR "linolenic acid" OR "linoleic acid" OR "linoleic acid" OR "linoleic acid" OR "docosahexaenoic acid\*" OR "Eicosapentaenoic Acid\*" OR "gamma-Linolenic Acid\*" OR (MH "Arachidonic Acids+") OR (MH "Ascorbic Acid Deficiency+") OR pufa OR pufas OR "alpha-linolenic acid\*" OR (MH "alpha-Linolenic Acid") OR (MH "Linolenic Acids+")

#5 - (MH "Vitamins") OR (MH "Vitamin B6 Deficiency") OR (MH "Vitamin B Deficiency") OR (MH "Vitamin B12 Deficiency") OR (MH "Vitamin D Deficiency") OR (MH "Vitamin A Deficiency") OR (MH "Vitamin K Deficiency") OR (MH "Vitamin E Deficiency") OR (MH "Riboflavin Deficiency") OR (MH "Ascorbic Acid Deficiency") OR (MH "Vitamin K") OR (MH "Vitamin B Complex") OR (MH "Vitamin B12") OR (MH "Vitamin A") OR (MH "Ascorbic Acid") OR (MH "Vitamin D") OR (MH "Vitamin E") OR (MH "Vitamin K") OR (MH "Cholecalciferol") OR (MH "Ergocalciferols") OR (MH "Iodine") OR (MH "Iodine Deficiency") OR (MH "Selenium") OR (MH "Oligosaccharides") OR "Vitamin B Complex" OR "vitamin b12" OR "vitamin b 12" OR "vitamin b 12" OR "vitamin c" OR "vitamin d" OR "ascorbic acid\*" OR choline OR "vitamin a" OR "vitamin e" OR "vitamin d" OR "vitamin k" OR retinol\* OR tocopherol\* OR cholecalciferol\* OR ergocalciferol\* OR quantity OR quality))

#6 - #1 AND #2

#7 - #3 OR #4 OR #5

#8 - #6 AND #7

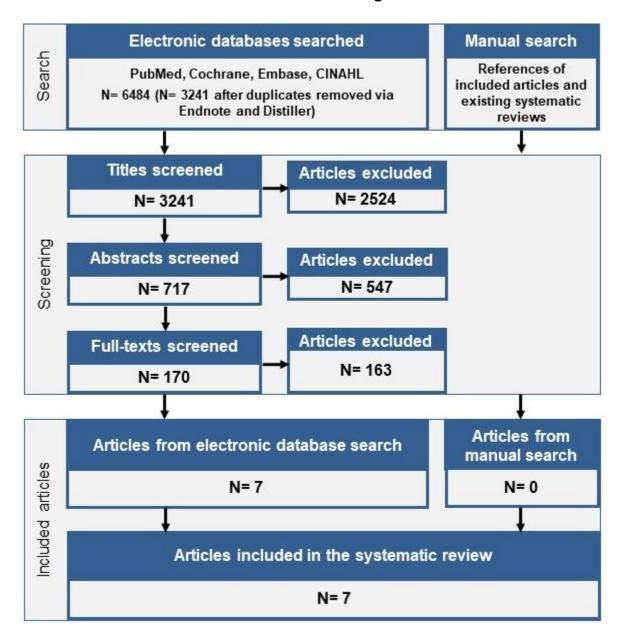
#9 - #8 NOT (MH "Literature Review" OR MH "Meta Analysis" OR MH "Systematic Review" OR MH "News" OR MH "Retracted Publication" OR MH "Retraction of Publication)

Filters: Published Date: 20000101 - 20191114, English Language; Human

## LITERATURE SEARCH AND SCREENING RESULTS

The flow chart (**Figure 2**) below illustrates the literature search and screening results for articles examining the systematic review question. After the initial electronic database search (January 2000-July 2019), an updated search was conducted to also capture macronutrient distribution articles (January 2000-November 2019). The results of both electronic database searches, after removal of duplicates, were screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles met the inclusion criteria for the systematic review question depicted. Refer to **Table 8** for the rationale for exclusion for each excluded full-text article. A manual search was done to find articles that were not identified when searching the electronic databases; all manually identified articles are also screened to determine whether they meet criteria for inclusion.

Figure 2. Flow chart of literature search and screening results



## **Excluded articles**

The table below lists the articles excluded after full-text screening, and includes rationale for the categories of inclusion and exclusion criteria (see Table 7) that studies were excluded based on. At least one reason for exclusion is provided for each article, though this may not reflect all possible reasons for exclusion. Information about articles excluded after title and abstract screening is available upon request.

Table 8. Articles excluded after full text screening with rationale for exclusion

	Citation	Rationale
1.	Agostoni, C, Marangoni, F, Grandi, F, Lammardo, AM, Giovannini, M, Riva, E, Galli, C. Earlier smoking habits are associated with higher serum lipids and lower milk fat and polyunsaturated fatty acid content in the first 6 months of lactation. European Journal of Clinical Nutrition. 2003. 57:1466-1472. doi:10.1038/sj.ejcn.1601711.	Comparator
2.	Alberti-Fidanza, A, Burini, G, Perriello, G. Total antioxidant capacity of colostrum, and transitional and mature human milk. J Matern Fetal Neonatal Med. 2002. 11:275-9. doi:10.1080/jmf.11.4.275.279.	Intervention/Exposure
3.	Ali, MA, Strandvik, B, Palme-Kilander, C, Yngve, A. Lower polyamine levels in breast milk of obese mothers compared to mothers with normal body weight. J Hum Nutr Diet. 2013. 26 Suppl 1:164-70. doi:10.1111/jhn.12097.	Intervention/Exposure
4.	Alien, CM, Smith, AM, Clinton, SK, Schwartz, SJ. Tomato consumption increases lycopene isomer concentrations in breast milk and plasma of lactating women. J Am Diet Assoc. 2002. 102:1257-62. doi:10.1016/s0002-8223(02)90278-6.	Intervention/Exposure
5.	Andersen, SL. Iodine status in pregnant and breastfeeding women: a Danish regional investigation. Dan Med J. 2015. 62.	Study Design; Intervention/Exposure
6.	Anderson, NK, Beerman, KA, McGuire, MA, Dasgupta, N, Griinari, JM, Williams, J, McGuire, MK. Dietary fat type influences total milk fat content in lean women. J Nutr. 2005. 135:416-21. doi:10.1093/jn/135.3.416.	Comparator
7.	Antonakou, A, Chiou, A, Andrikopoulos, NK, Bakoula, C, Matalas, AL. Breast milk tocopherol content during the first six months in exclusively breastfeeding Greek women. Eur J Nutr. 2011. 50:195-202. doi:10.1007/s00394-010-0129-4.	Intervention/Exposure
8.	Antonakou, A, Skenderi, KP, Chiou, A, Anastasiou, CA, Bakoula, C, Matalas, AL. Breast milk fat concentration and fatty acid pattern during the first six months in exclusively breastfeeding Greek women. Eur J Nutr. 2013. 52:963-73. doi:10.1007/s00394-012-0403-8.	Intervention/Exposure; Comparator
9.	Arora, M, Ettinger, AS, Peterson, KE, Schwartz, J, Hu, H, Hernández-Avila, M, Tellez-Rojo, MM, Wright, RO. Maternal dietary intake of polyunsaturated fatty acids modifies the relationship between lead levels in bone and breast milk. Journal of Nutrition. 2008. 138:73-79.	Intervention/Exposure

	Citation	Rationale
10.	Aumeistere, L, Ciprovica, I, Zavadska, D, Andersons, J, Volkovs, V, Celmalniece, K. Impact of Maternal Diet on Human Milk Composition Among Lactating Women in Latvia. Medicina (Kaunas). 2019. 55. doi:10.3390/medicina55050173.	Intervention/Exposure
11.	Aumeistere, L, Ciproviča, I, Zavadska, D, Volkovs, V. Fish intake reflects on DHA level in breast milk among lactating women in Latvia. International Breastfeeding Journal. 2018. 13:N.PAG-N.PAG. doi:10.1186/s13006-018-0175-8.	Intervention/Exposure
12.	Azad, MB, Robertson, B, Atakora, F, Becker, AB, Subbarao, P, Moraes, TJ, Mandhane, PJ, Turvey, SE, Lefebvre, DL, Sears, MR, Bode, L. Human Milk Oligosaccharide Concentrations Are Associated with Multiple Fixed and Modifiable Maternal Characteristics, Environmental Factors, and Feeding Practices. J Nutr. 2018. 148:1733-1742. doi:10.1093/jn/nxy175.	Population
13.	Baatenburg de Jong, R, Bekhof, J, Roorda, R, Zwart, P. Severe nutritional vitamin deficiency in a breast-fed infant of a vegan mother. Eur J Pediatr. 2005. 164:259-60. doi:10.1007/s00431-004-1613-8.	Study Design
14.	Baheiraei, A, Shamsi, A, Khaghani, S, Shams, S, Chamari, M, Boushehri, H, Khedri, A. The effects of maternal passive smoking on maternal milk lipid. Acta Med Iran. 2014. 52:280-5.	Intervention/Exposure
15.	Barrera, C, Valenzuela, R, Chamorro, R, Bascunan, K, Sandoval, J, Sabag, N, Valenzuela, F, Valencia, MP, Puigrredon, C, Valenzuela, A. The Impact of Maternal Diet during Pregnancy and Lactation on the Fatty Acid Composition of Erythrocytes and Breast Milk of Chilean Women. Nutrients. 2018. 10. doi:10.3390/nu10070839.	Intervention/Exposure
16.	Bascunan, KA, Valenzuela, R, Chamorro, R, Valencia, A, Barrera, C, Puigrredon, C, Sandoval, J, Valenzuela, A. Polyunsaturated fatty acid composition of maternal diet and erythrocyte phospholipid status in Chilean pregnant women. Nutrients. 2014. 6:4918-34. doi:10.3390/nu6114918.	Intervention/Exposure; Outcome
17.	Bertschi, I, Collomb, M, Rist, L, Eberhard, P, Sieber, R, Bütikofer, U, Wechsler, D, Folkers, G, von Mandach, U. Maternal dietary Alpine butter intake affects human milk: fatty acids and conjugated linoleic acid isomers. Lipids. 2005. 40:581-587.	Intervention/Exposure
18.	Bobiński, R, Mikulska, M, Mojska, H, Ulman-Włodarz, I, Sodowska, P. Pregnant women's diet composition and transitional milk fatty acids: factor analysis. Ginekologia polska. 2015. 86:113-118.	Intervention/Exposure; Outcome
19.	Bode, L. Human Milk Oligosaccharides at the Interface of Maternal-Infant Health. Breastfeed Med. 2018. 13:S7-s8. doi:10.1089/bfm.2018.29073.ljb.	Study Design
20.	Boniglia, C, Carratu, B, Chiarotti, F, Giammarioli, S, Sanzini, E. Influence of maternal protein intake on nitrogen fractions of human milk. Int J Vitam Nutr Res. 2003. 73:447-52. doi:10.1024/0300-9831.73.6.447.	Intervention/Exposure

	Citation	Rationale
21.	Bopp, M, Lovelady, C, Hunter, C, Kinsella, T. Maternal diet and exercise: effects on long-chain polyunsaturated fatty acid concentrations in breast milk. J Am Diet Assoc. 2005. 105:1098-103. doi:10.1016/j.jada.2005.04.004.	Intervention/Exposure
22.	Buntuchai, G, Pavadhgul, P, Kittipichai, W, Satheannoppakao, W. Traditional Galactagogue Foods and Their Connection to Human Milk Volume in Thai Breastfeeding Mothers. J Hum Lact. 2017. 33:552-559. doi:10.1177/0890334417709432.	Intervention/Exposure
23.	Burtseva, T, Solodkova, I, Savvina, M, Dranaeva, G, Shadrin, V, Avrusin, S, Sinelnikova, E, Chasnyk, V. Dietary intakes of energy and macronutrients by lactating women of different ethnic groups living in Yakutia. Int J Circumpolar Health. 2013. 72. doi:10.3402/ijch.v72i0.21519.	Intervention/Exposure
24.	Butts, CA, Hedderley, DI, Herath, TD, Paturi, G, Glyn-Jones, S, Wiens, F, Stahl, B, Gopal, P. Human Milk Composition and Dietary Intakes of Breastfeeding Women of Different Ethnicity from the Manawatu-Wanganui Region of New Zealand. Nutrients. 2018. 10. doi:10.3390/nu10091231.	Intervention/Exposure
25.	Bzikowska-Jura, A, Czerwonogrodzka-Senczyna, A, Jasinska-Melon, E, Mojska, H, Oledzka, G, Wesolowska, A, Szostak-Wegierek, D. The Concentration of Omega-3 Fatty Acids in Human Milk Is Related to Their Habitual but Not Current Intake. Nutrients. 2019. 11. doi:10.3390/nu11071585.	Intervention/Exposure
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